ARCHIVES

OF

THE MIDDLESEX HOSPITAL

VOLUME III

Third Report

FROM THE

Cancer Research Laboratories

THE CANCER WING, THE MIDDLESEX HOSPITAL

London
MACMILLAN AND CO., LIMITED
NEW YORK: THE MACMILLAN COMPANY
1904

ARCHIVES

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The Middlesex Hospital

VOLUME III

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THESE Archives are published with the object of recording work done in the Wards, Laboratories, and Special Departments of The Middlesex Hospital, and will contain contributions upon subjects connected with—

1. Clinical Medicine and Surgery,
2. The Investigation of Cancer,
3. Research carried on in the Pathological and Bacteriological Laboratories, and
4. The work of the Special Departments of the Hospital and School.

It is hoped that the publication of this Work will advance the Science of Medicine, and that the monographs and original observations contained in the Archives will give the volumes a permanent value.

It is intended to issue not less than four volumes annually.

Those volumes of the Archives which deal with the general work of the Hospital, its Laboratories, and Special Departments, will be produced under the direction of an Editorial Committee, consisting of:—

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Volumes dealing with the special work of the Cancer Research Laboratories will be produced under the direction of the Cancer Investigation Committee. Hon. Secretary, W. S. Lazarus-Barlow, Esq., M.D., F.R.C.P.

The price of each Volume will necessarily vary with the cost of production, but in the belief that many past Students of the Hospital and others will desire to possess them, it has been decided to accept a nominal Subscription of half a guinea per annum for the whole series.

Subscriptions should be made payable to the Secretary-Superintendent, The Middlesex Hospital, London, W.

E. E. Pardinson

ARCHIVES

OF

THE MIDDLESEX HOSPITAL

VOLUME III

Third Report

FROM THE

Cancer Research Laboratories

EDITED FOR THE CANCER INVESTIGATION COMMITTEE

BY

W. S. LAZARUS-BARLOW, M.D., F.R.C.P.,

DIRECTOR OF THE CANCER RESEARCH LABORATORIES; MEMBER OF THE GERMAN COMMITTEE FOR THE INVESTIGATION OF CANCER; FORMERLY PATHOLOGIST AND LECTURER ON PATHOLOGY AT THE WESTMINSTER HOSPITAL.

London
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EDITORIAL NOTE.

IN the present Volume are included the details of all cases of malignant disease admitted into the Hospital—whether the General Wards or the Special Cancer Wards—during the year 1903, together with a number of Papers written by workers in the Laboratories. In addition, Papers on various aspects of Cancer have been contributed by other gentlemen connected with the Hospital who are not directly concerned with the Cancer Department, and in one instance by a gentleman (Dr. D. W. SUTHERLAND) not connected with the Hospital at all. The value and the subject of Dr. SUTHERLAND'S Paper sufficiently justifies our departure from the rule not to admit to the "Archives" work done elsewhere than at The Middlesex Hospital.

The Committee wishes to express its sincere thanks to the Weekly Board of St. George's Hospital for the cordial manner in which they gave access to their valuable records for the purpose of collecting the St. George's Hospital statistics on Cancer. When it is recognized that the investigation of the records occupied Dr. GORDON TAYLOR daily for nearly two months, the value of the concession becomes apparent.

In conclusion, it is my pleasant duty to thank all those who have been associated with me in the Laboratories during this the first year of my tenure of office as Director. If I mention Mr. W. T. HILLIER in particular, it is that he rendered me the most ready help during the months immediately succeeding my election. His resignation on being appointed First Assistant in the Clinical and Bacteriological Laboratories deprived me of a most valuable and most agreeable colleague.

W. S. LAZARUS-BARLOW.

THE MIDDLESEX HOSPITAL, LONDON.

July 1st, 1904.

NOTICE.

In the following Pages, excepting where an asterisk (*) *is placed, or where the context makes it clear that such is not the case,* EVERY DIAGNOSIS OF MALIGNANT DISEASE HAS BEEN MADE AS THE RESULT OF MICROSCOPIC EXAMINATION.

W. S. L.-B.

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FROM THE

CANCER RESEARCH LABORATORIES.

TABULATED SYNOPSES OF THE POST-MORTEM EXAMINATIONS AND OPERATIONS IN CASES OF MALIGNANT DISEASE DURING THE YEAR 1903.

In the following Tables are given the results of the Macroscopic and Microscopic Examinations made in the Cancer Research Laboratories during 1903, upon material obtained from the Post-mortem Room and the Operating Theatre. In seven cases the same individual appears in both lists, having died in the Hospital subsequent to operation. Subtracting these from the combined totals of Tables I. and II., and adding the ten cases in Table III., it appears that malignant disease was recognized in 279 patients during the year. The total number of admissions into Hospital during the same period was 4095.

It may be repeated here in respect of all cases, that organs in which the diagnosis was made macroscopically, but in which microscopic examination was wanting, are distinguished by an asterisk (*).

TABLE 1.—

		0—5		6—10		11—15		16—20		21—25		26—30		31—35		36—40	
		M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
	CARCINOMA.																
ALIMENTARY SYSTEM.	Lip . . . . Squamous	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Cheek . . . . Squamous	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	...
	Tongue and floor of mouth Squamous	...	...	...	...	...	...	...	...	...	...	..	...	...	...	...	...
	Tonsil . . . Squamous	..	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Pharynx . . . Squamous	...	...	...	...	...	...	...	...	...	...		...	...	...	...	...
	Œsophagus, Upper part Squamous	...	...	...	...	..	...	...	...	...	...	...	...	...	...	...	...
	Middle part Squamous	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Lower part { Squamous	...	...	...	...	. .	...	...	...	...	...	...	...	...	...	...	...
	Lower part { Columnar	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Stomach { Spheroidal	...	...	...	...	...	...	...	...	...	...	...	...	...	1	2	...
	Cardiac end { Transitional	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Cardiac end { Columnar		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Middle . Spheroidal	...	...	...	...	...	...	...	...	...	...	..	...	...	...	...	...
	Pyloric end { Spheroidal	...	...	...	...	...	...	...	...	...	...	...	...	...	1	...	...
	Pyloric end { Transitional	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Pyloric end { Columnar	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Colon: Ascending . Columnar	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Splenic Flexure . Columnar	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Sigmoid Flexure Columnar	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Rectum . . { Spheroidal		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Rectum . . { Columnar	...	...	...	...	...	...	...	...	...	...	...	1	...	...	...	1
	Liver and Bile Passages { Spheroidal	..	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Liver and Bile Passages { Columnar	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Pancreas . . . . Columnar	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
URO-GENITAL SYSTEM.	Adrenal . . . Spheroidal	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Ureter . . . Transitional	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Bladder and Urethra Squamous	...	..	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	Uterus, corpus . . Spheroidal	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
	cervix . . { Squamous	..	...	...	...	...	...	...	...	...	...	...	...	...	1	...	4
	cervix . . { Columnar	...	...	...	...	...	...	...	...	...	..	...	...	...	...	...	...
	Vagina . . . Squamous	...		...	...	...	...	...	...	...	...	...	...	...	1	...	...
	Vulva . . . Squamous	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Breast . . . . . Spheroidal		...	...	...	...	...	...	...	...	...	...	...	...	1	...	3
Other Sites . . . . Squamous		...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
Proliferating Cystadenoma . . .		...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...
	SARCOMA.																
Mixed-cell			...	...	...	...	...	...	Neck	...	...	...	...	...	...	...	Nasal
Round-cell		...	Orbit	...	...	...	...	An-trum	...	...	...	...	...	...	Stom-ach	Kidney, Larynx, Stomach	...
Spindle-cell		...	...	...	...	...	...	...	...	...	...	...	...	...	Os frontis	...	...
Lympho-Sarcoma		...	...	...	...	...	...	...	Neck	...	...	...	...	...	...	...	...
Endothelioma . . . { Lymphatic		...	...	...	...	...	...	...	...	...	...	...	Tym-panum	...	...	...	...
Endothelioma . . . { Hæmal		...	..	...	...	...	...	...	...	...	...	...	...	...	...	...	...

Post-Mortem Cases.

41–45		46–50		51–55		56–60		61–65		66–70		71–75		76–80		81–85		Total	
M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
1	...	...	...	...	...	...	...	1	...	...	...	...	...	...	...	..	...	2	0
...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	2	0
...	...	...	...	3	...	3	...	...	...	1	...	...	...	...	...	...	...	7	0
..	...	..	...	...	...	...	...	...	...	1	...	...	...	...	...	...	...	1	0
...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0
...	...	...	...	1	...	1	...	1	...	...	...	...	...	...	...	...	...	3	0
...	...	1	...	..	...	1	...	...	...	1	...	...	...	...	...	...	...	3	0
...	...	1	...	...	...	...	...	1	...	1	...	...	...	...	...	...	...	3	0
...	...	...	...	1	...	...	...	...	...	...	.	...	...	...	...	...	..	1	0
1	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	3	1
...	...	...	...	...	...	...	...	...	1	...	...	...	...	...	...	...	...	0	1
...	...	...	...	...	...	...	...	...	...	...	1	...	...	...	...	...	...	0	1
1	...	...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	2	0
...	...	...	...	1	...	1	...	1	1	...	...	...	...	...	...	...	...	3	2
...	...	...	...	...	1	...	...	...	...	...	...	...	...	...	..	...	...	0	1
...	...	...	...	...	...	1	...	...	...	2	...	...	...	...	...	...	...	3	0
1	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	2	0
...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0
...	...	...	...	1	...	1	...	...	...	...	...	...	...	...	...	...	...	2	0
...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0
...	...	...	...	...	1	3	...	1	...	...	...	...	...	1	...	...	...	4	4
...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0
...	...	...	...	...	...	...	...	...	1	1	...	...	...	...	...	...	..	1	1
...	...	.	...	...	...	1	...	...	...	...	1	...	...	...	...	...	...	1	1
...	...	1	...	...	...	...	...	...	...	..	...	...	...	...	...	...	...	1	0
...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0
...	1	2	...	...	...	...	...	...	1	...	...	...	...	...	...	...	...	2	2
...	1	...	...	...	...	...	...	...	1	...	...	...	...	...	...	...	...	0	2
...	2	.	4	...	2	...	5	...	...	...	1	...	...	...	...	...	...	0	19
..	2	...	.	...	...	...	...	...	...	...	...	...	...	...	...	...	...	0	2
...	...	...	...	...	...	...	1	..	...	...	1	...	...	...	...	...	...	0	3
...	..	...	...	...	...	...	1	...	...	...	...	...	...	...	...	...	...	0	1
...	5	...	2	...	1	...	2	...	1	...	1	...	...	...	...	...	...	0	16
...	...	...	...	. .	...	1	...	...	...	...	...	...	...	...	...	...	...	1	0
...	...	...		...	...	1	...	...	...	...	...	...	...	...	...	...	...	1	1
...	...	...		Lymph Glands	...	Stomach	...	...	Nasal	...	...	...	...	...	...	...	...	2	3
...	...	...	...	...	...	...	...	...	...	Larynx	...	...	...	.	...	...	...	5	2
.	...	...	...	...	Ovary	...	...	...	...	...	...	...	...	...	...	...	...	0	2
Mediastinum	...	...	.	...	...	...	Mediastinum Breast	Mediastinum Tongue	..	...	...	...	...	...	...	...	...	2	4
External Ear, Tongue	...	...	.	...	...	...			...	...	...	...	...	...	...	...	..	3	2
...	...	Tongue	..	...	...	...	...	...	...	...	...	...	...	...	...	..	...	1	0
																		66	71

TABLE II.—

		16—20		21—25		26—30		31—35		36—40		41—45	
		M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
	CARCINOMA.												
	Face . . Squamous	...	...	...	...	...	...	1	...	...	...	1	...
ALIMENTARY CANAL.	Lip . . Squamous	...	...	...	...	...	...	...	...	...	...	...	...
	Tongue . Squamous	...	...	...	...	...	...	...	1	...	...	...	...
	Intestine — Spheroidal	...	...	...	...	...	...	...	...	...	...	...	...
	Intestine — Columnar	...	...	1 (rectum)	...	...	...	...	...	...	1 (rectum)	...	...
	Generative System — Squamous	...	...	...	...	...	...	...	...	...	1 (cervix)	...	3 (vulva, vulva, vagina)
	Generative System — Spheroidal	...	...	...	...	...	...	...	...	...	...	...	...
	Generative System — Columnar	...	...	...	...	...	...	...	...	...	...	...	...
	Breast — Spheroidal	...	...	...	...	...	...	...	3	...	5	...	2
	Breast — Columnar	...	...	...	...	...	...	...	...	...	...	...	1
	Other Sites . Squamous	...	...	...	...	...	...	...	1 (knee)	...	...	...	...
	RODENT CANCER.	...	...	...	...	...	...	...	...	...	...	...	...
	PROLIFERATING CYSTADENOMA .	...	...	...	...	...	...	...	...	...	...	...	...
	SARCOMA.												
	Mixed-cell	...	...	1 (spermatic cord)	...	1 (muscle of thigh)	...	...	3 (breast, axilla, osfrontis)	...	...	...	...
	Round-cell	...	...	...	...	...	...	...	...	...	...	...	...
	Spindle-cell	...	...	...	...	...	...	...	...	1 (cheek)	...	...	1 (skin)
	Giant-cell	1 (femur)	...	...	1 (jaw)	...	...	...	...	...	...	...	...
	Myxo-sarcoma	...	...	...	...	...	...	...	...	...	...	...	...
	Endothelioma — Lymphatic .	...	...	...	...	...	...	...	...	...	...	1 (tongue)	...
	Endothelioma — Hæmal . .	...	...	...	...	...	...	...	...	...	...	...	...
	NON-MALIGNANT.	1	2	...	1	...	2	1	1	...	...	...	3

Operation Cases.

46—50		51—55		56—60		61—65		66—70		71—75		76—80		81—85		Total	
M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
...	...	1	...	...	...	2	...	...	1	...	...	...	...	...	...	5	1
1	...	...	...	...	...	2	...	1	...	1	...	1	...	...	...	6	0
2	...	2	...	...	1	...	...	1	...	1	...	...	...	...	...	6	2
1 (rectum)	...	1 (rectum)	...	...	...	...	...	...	...	...	...	...	...	...	...	2	0
...	...	2 (colon, rectum)	...	...	...	...	...	...	...	...	...	...	...	...	...	3	1
...	...	...	1 (cervix)	1 (penis	...	...	...	...	...	...	...	...	...	...	...	1	5
...	...	1 (prostate)	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0
...	1 (uterus)	...	...	...	...	...	...	...	...	...	...	...	...	...	...	0	1
...	10	1	7	...	7	...	2	...	2	...	...	...	...	...	...	1	38
...	...	...	...	...	...	...	2	...	...	...	...	...	...	...	...	0	3
...	...	...	...	...	...	...	2 (foot, ? site)	...	1 (scalp)	...	...	...	...	...	...	0	4
...	1 (orbit)	...	...	...	...	1 (? site)	1 (cheek)	...	...	...	...	...	...	...	1 (vulva)	1	3
...	1 (ovary)	...	...	...	...	...	...	...	...	...	...	...	...	...	...	0	1
...	...	...	...	...	1 (skin)	...	1 (tibia)	...	...	...	...	...	...	...	...	2	5
1 (mandible)	...	...	...	...	...	...	1 (breast)	...	...	...	...	...	...	...	...	1	1
...	...	1 (maxilla)	.	...	.	...	...	...	...	...	...	...	...	...	...	2	1
...	...	.	...	..	...	...	...	...	...	...	...	...	...	...	...	1	1
...	...	...	...	...	.	..	...	1 (kidney)	...	...	..	...	1 (nose)	...	...	1	1
...	..	...	...	...	...	...	...	...	...	...	...	...	...	...	...	1	0
...	...	...	...	...	...	...	..	...	1 (breast)	...	...	..	...	...	...	0	1
Total Malignant Operation Cases (Carcinoma—Male 26, Female 59 / Sarcoma ,, 8, ,, 10)																34	69
...	6	3	1	..	5	1	3	1	2	...	1	1	...	...	.	8	28
Total Operation Cases...																42	97

TABLE III.

OPERATION CASES ENTERED IN THE REGISTER OF THE CLINICAL LABORATORY, BUT NOT EXAMINED IN THE CANCER RESEARCH LABORATORY.

No.	Name.	Age.	Site of growth.	Diagnosis.
3	Adelina B. ..	36	Glands	Spheroidal cell carcinoma
885	Marie M. ..	?	Axillary gland	do.
746	John B. ..	50	Upper lip	Squamous cell carcinoma
123	Thomas G. ..	65	Palate	do.
974	Edward T. ..	34	Gland in parotid region	do.
399	William B. ..	50	Submaxillary gland ..	do.
686	Kate F. ..	43	Uterus	do.
529	Henry B. ..	58	Tissue from throat ..	"Probably malignant."
311	Joseph B. ..	47	Hernial sac	do.
625	Charlotte H.	39	Ovarian cyst	"Probably myxo-sarcoma"

NOTE.—The above cases are given in order to present a complete list of all the recognized malignant disease in the Hospital during 1903. They are not included in any of the other lists.

TABLE IV.

No.	Cancer Register Number.	Sex.	Age at death.	Nature of new growth and part primarily affected.	Secondary formations of new growth.	Morbid changes present other than those apparently due to new growth.	(i) Congenital abnormalities. (ii) General remarks.	(i) Date of admission. (ii) Date of death. (iii) Duration of disease on admission. (iv) Surgical operation, if any.
1	T.T. 249 03	M	64	Squamous-celled carcinoma of lower lip (left half) extending to whole of upper lip, and invading subjacent salivary gland.	Lymph-gland.	*Stomach :* small fibroma in posterior wall. Calcification of lymph-glands in left inguinal region. Scar on glans penis. *Testes :* fibrotic. Aorta, coronary and splenic arteries greatly calcified.	(ii) Wasting.	(i) 7 Sept. 1903 (ii) 23 Oct. 1903
2	R.T.R. 188 03	M	41	Squamous-celled carcinoma of left angle of mouth.	Cervical* mesenteric, and mediastinal lymph-glands, liver, lung, right adrenal, right kidney, pancreas, pleura, heart, manubrium sterni.*	Small vaginal hydrocele on each side.	(ii) Some wasting.	(i) 13 June 1903 (ii) 8 Aug. 1903
3	E.R. 217/03	M	39	Squamous-celled carcinoma of left cheek, invading left side of root of tongue.	Cervical lymph-glands.*	*Lungs :* broncho-pneumonia ; apical adhesions.	(ii) Great wasting.	(i) 29 Aug. 1903 (ii) 15 Sept. 1903
4	H.W. 211 03	M	55	Squamous-celled carcinoma of left cheek (outer surface), infiltrating root of tongue, pharynx, and trachea.	Sublingual lymph-glands, left arytenoepiglottidean fold, right kidney.	*Larynx :* œdema.	(ii) Wasting and pigmentation.	(i) 11 Aug. 1903 (ii) 6 Sept. 1903

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5	E.H. 78/03	M	52	Squamous-celled carcinoma of tongue.	Left submaxillary lymph-glands. Anterior mediastinum and pleura.	*Lungs:* slight bronchiectasis. Vaginal hydrocele both sides.	(i) Duodenal pouch (5 cc. capacity). (ii) Some wasting.	(i) 7 Feb. 1903 (ii) 15 April 1903 (iv) Removal of tongue
6	H.J. 186/03	M	60	Squamous-celled carcinoma of right side of tongue.	Anterior part of tongue, lungs, cervical lymph-glands of both sides.	*Lungs:* caseous and calcareous disseminated nodules (tuberculous)	(ii) Slight wasting.	(i) 30 June 1903 (ii) 7 Aug. 1903
7	S.S. 227/03	M	60	Squamous-celled carcinoma of tongue, right border.	Submaxillary lymph-gland, left side of tongue.	*Lungs:* œdema and broncho-pneumonia in both organs.	(ii) Hosp. p.m. 195. Some wasting.	(i) 17 Sept. 1903 (ii) 29 Sept. 1903 (iv) Partial excision of tongue
8	G.C. 90/03	M	66	Squamous-celled carcinoma of floor of mouth, extending into lower jaw.	Cervical lymph-glands, right lung, skin over mandible.*	*Heart:* Aortic cusps calcified. Sacculated aneurysm of arch of aorta and marked calcification. *Intestines:* ulcer of first part of duodenum.	(ii) Great wasting.	(i) 18 March 1903 (ii) 29 April 1903
9	S.G.C. 236/03	M	54	Squamous-celled carcinoma of root of tongue.	Cervical lymph-glands.	*Lungs:* tuberculosis, also tuberculosis of mediastinal glands.	(ii) Very marked wasting.	(i) 20 April 1903 (ii) 4 Oct. 1903
10	W.B. 187/03	M	55	Squamous-celled carcinoma of root of tongue.	Cervical lymph-glands, both sides.	*Lungs:* cicatrization of right apex. *Colon:* 3 simple polypi.	(ii) Some wasting.	(i) 17 July 1903 (ii) 8 Aug. 1903
11	J.L. 135/03	M	58	Squamous-celled carcinoma of root of tongue, left side.	Cervical and submaxillary* lymph-glands. Small nodules between tongue and larynx.	*Larynx:* œdema of left ary-epiglottic fold. *Lungs:* septic broncho-pneumonia. *Heart:* calcification of right coronary artery. *Liver:* cirrhosis. *Intestines:* polypus at ileo-cæcal valve.	(ii) Well nourished.	(i) 1 May 1903 (ii) 12 June 1903

12	N.C. 164 03	M	68	Carcinoma* of left tonsil, extending to soft palate and pharynx.	Cervical lymph-glands.*	*Lungs:* calcareous deposits at right apex. *Adrenal:* adenoma.	(ii) Hosp. p.m. 177. Some wasting.	(i) 29 June 1903 (ii) 3 July 1903
13	D.A. 177 03	M	48	Squamous-celled carcinoma of pharynx, left side.	Cervical lymph-glands,* liver.*	*Heart:* Aortic valve incompetent. *Lungs:* fibrous nodules at apices.	(ii) Some jaundice. Death from hæmorrhage.	(i) 23 April 1903 (ii) 21 July 1903
14	T.B. 181 03	M	51	Squamous-celled carcinoma of upper part of œsophagus, infiltrating vertebral column and trachea.	None.	.. ..	(ii) Hosp. p.m. 142. Extreme wasting.	(i) 21 July 1903 (ii) 28 July 1903 (iv) Gastrostomy
15	W.B. 94 03	M	56	Squamous-celled carcinoma of œsophagus, opening by sinus below thyroid cartilage.	Posterior mediastinal lymph-glands, left lung.*	*Stomach:* occupied by a perfect cast of its interior of clotted blood.	(i) Small Meckel's diverticulum. (ii) Hosp. p.m. 67. No wasting.	(i) 23 April 1903 (ii) 1 May 1903
16	J.K. 195 03	M	61	Squamous-celled carcinoma of upper part of œsophagus.	Lymph-glands.	.. ..	(ii) Hosp. p.m. 163. Marked wasting.	(i) 1 Aug. 1903 (ii) 16 Aug. 1903 (iv) Gastrostomy
17	W.D. 196 03	M	47	Squamous-celled carcinoma of middle of œsophagus, invading trachea.	Œsophageal lymph-glands.	*Lungs:* intense broncho-pneumonia.	(ii) Hosp. p.m. 165. Much wasting.	(i) 14 Aug. 1903 (ii) 18 Aug. 1903 (iv) Gastrostomy
18	F.W. 207 03	M	58	Squamous-celled carcinoma of middle part of œsophagus, invading the pericardium, bronchial lymph-glands, right lobe of thyroid body, trachea, and left lung.	Clavicular lymph-gland.*	.. ..	(ii) Hosp. p.m. 174. Marked wasting.	(i) 27 Aug. 1903 (ii) 1 Sept. 1903
19	F.D. 65 03	M	67	Squamous-celled carcinoma of œsophagus (no cell nests), invading trachea.	None.	*Heart:* mitral valve thickened.	(ii) Hosp. p.m. 47. Fairly well nourished.	(i) 23 March 1903 (ii) 24 March 1903

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20	W.P. 95/03	M	48	Squamous-celled carcinoma of œsophagus, extending to stomach and left lobe of liver.	Liver,* abdominal lymph-glands.	*Lungs:* pneumonia right side. *Pleura:* 4 ozs. of pus in right cavity.	(ii) Hosp. p.m. 68. Marked wasting.	(i) 10 Feb. 1903 (ii) 1 May 1903
21	G.C. 198/03	M	63	Squamous-celled carcinoma of lower end of œsophagus.	Œsophageal and portal lymph-glands.	.. ..	(ii) Hosp. p.m. 167. Wasting.	(i) 6 Aug. 1903 (ii) 25 Aug. 1903
22	D.T. 93/03	M	66	Squamous-celled carcinoma of œsophagus, extending to stomach.	.. .. ..	*Liver:* cirrhosis.	(ii) Hosp. p.m. 65. Well nourished.	(i) 19 March 1903 (ii) 30 April 1903
23	H.J. 20/03	M	51	Columnar-celled carcinoma of œsophagus.	Supra-clavicular, mediastinal,* and portal* lymph-glands, lungs.	*Lungs:* cicatrization at each apex.	(ii) Some wasting.	(i) 20 Sept. 1902 (ii) 27 Jan. 1903
24	J.B. 37/03	M	38	Spheroidal-celled carcinoma of cardiac end of stomach.	Mediastinal lymph-glands, liver, spleen.	*Stomach:* near pylorus is seen a circular cicatrix. *Lungs:* broncho-pneumonia in right; left shrunken, caseous nodules at left apex. *Pleura:* empyema on left side, communicating with stomach. *Gall-bladder:* contains several calculi.	(ii) Hosp. p.m. 27. Wasting.	(i) 1 Dec. 1902 (ii) 12 Feb. 1903
25	T.D. 113/03	M	40	Spheroidal-celled carcinoma of cardiac end of stomach.	Mediastinal, bronchial, mesenteric, and retro-peritoneal lymph-glands, right second—fifth ribs, liver, pancreas, lumbar vertebra.	*Lungs:* right broncho-pneumonia and calcareous nodule.	(ii) Hosp. p.m. 81. Marked wasting.	(i) 16 March 1903 (ii) 20 May 1903

26	A.H. 255/03	M	43	Spheroidal-celled carcinoma of cardiac end of stomach; colloid.	Cœliac lymph-glands, pericardium, pleura, peritoneum and omentum, muscular wall of small intestine.	Peritoneal effusion.	(ii) Hosp. p.m. 210. Wasting.	(i) 2 Oct. 1903 (ii) 27 Oct. 1903
27	E.B. 202/03	F	31	Spheroidal-celled carcinoma of cardiac end of stomach.	Retro-peritoneal lymph-glands, liver, lung, pericardium,* thyroid-gland,* receptaculum chyli,* and thoracic duct.*	*Uterus:* erosions of cervix. *Pleuræ:* effusions into both cavities.	(ii) Hosp. p.m. 171. Body well nourished.	(i) 21 Aug. 1903 (ii) 28 Aug. 1903
28	E.B. 15/03	F	64	Transitional-celled carcinoma of cardiac end of stomach.	None.	*Heart:* foramen ovale patent. Pus in peritoneal cavity. Small polypus in rectum.	(ii) Great wasting.	(i) 15 Nov. 1902 (ii) 25 Jan. 1903
29	A.F. 228/03	F	69	Columnar-celled carcinoma of cardiac end of stomach.	None.	*Lungs:* evidence of old tuberculosis.	(ii) Hosp. p.m. 189. Wasting.	(i) 10 Sept. 1903 (ii) 25 Sept. 1903
30	F.B. 229/03	M	45	Spheroidal-celled carcinoma of stomach (middle); colloid.	Abdominal lymph-glands,* liver, peritoneum.	*Lungs:* tuberculous cavities in both. Chronic peritonitis with effusion.	(ii) Hosp. p.m. 193. Wasting.	(i) 11 Sept. 1903 (ii) 28 Sept. 1903
31	W.F. 144/03	M	57	Spheroidal-celled carcinoma of the stomach, involving peritoneum, omentum, and pancreas.	Abdominal lymph-glands and mesentery, liver, pancreas.	Purulent peritonitis. *Lungs:* cavity at left apex.	(ii) Hosp. p.m. 65. Deeply jaundiced.	(i) 4 June 1903 (ii) 18 June 1903
32	W.N. 116/03	M	55	Spheroidal-celled carcinoma of pyloric end of stomach.	Liver, gall-bladder, omentum,* pancreas.*	*Kidneys:* mulberry-shaped calculus in pelvis of each organ.	(ii) Hosp. p.m. 83. Body well nourished.	(i) 18 May 1903 (ii) 23 May 1903
33	J.F. 92/03	M	57	Spheroidal-celled carcinoma of pyloric end of stomach.	None.	Septic peritonitis.	(i) Meckel's diverticulum. (ii) Hosp. p.m. 64. No wasting.	(i) 23 March 1903 (ii) 27 April 1903 (iv) Gastro-jejunostomy

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34	J.D. 233/03	M	63	Spheroidal-celled carcinoma of pyloric end of stomach.	Stomach, peritoneum, and tissue surrounding left ureter, mesentery.	*Kidneys:* hydronephrosis on left side (peritoneal growth pressing on ureter).	(ii) Hosp. p.m. 198. Great wasting.	(i) 28 Sept. 1903 (ii) 30 Sept. 1903 (iv) Gastro-jejunostomy
35	M.M. 143/03	F	35	Spheroidal-celled carcinoma of pyloric end of stomach.	Cœliac lymph-glands, liver, abdominal wall.	Perforation of stomach, purulent peritonitis.	(ii) Hosp. p.m. 104. Extreme wasting (scar in right breast, scar in abdomen above umbilicus).	(i) 10 March 1903 (ii) 18 June 1903
36	E.V. 285/03	F	64	Spheroidal-celled carcinoma of pyloric end of stomach (colloid).	Peritoneum.	*Peritoneum:* chronic inflammation. Bronchial lymph-glands caseous	(ii) Much wasting.	(i) 14 Oct. 1903 (ii) 19 Dec. 1903 (iv) Gastro-jejunostomy
37	E.M. 191/03	F	53	Transitional-celled carcinoma of pyloric end of stomach, invading duodenum and pancreas.	Cœliac lymph-glands, liver.	Adenoma of thyroid gland. *Uterus:* cervical polypus.	(ii) Hosp. p.m. 158. Wasting.	(i) 9 June 1903 (ii) 10 Aug. 1903 (iv) Laparotomy
38	E.W. 242/03	M	59	Columnar-celled carcinoma of pyloric end of stomach, invading duodenum.	Lumbar, cœliac, and left supra-clavicular lymph-glands, thoracic duct, liver, right adrenal.	*Lungs:* cicatrization at the apices. *Heart:* aortic valve incompetent. Splenic vein thrombosed.	(i) Ileum and jejunum together measure only 14 feet (ii) Wasting.	(i) 18 Aug. 1903 (ii) 15 Oct. 1903
39	W.H.S. 170/03	M	66	Columnar-celled carcinoma of pyloric end of stomach,* extending to duodenum.	Portal lymph-gland.	.. ..	(ii) Hosp. p.m. 123. Marked wasting.	(i) 3 July 1903 (ii) 9 July 1903
40	W.A. 102/03	M	67	Columnar-celled carcinoma of pyloric end of stomach.	Colon, cœliac lymph-glands.*	Aorta very atheromatous and greatly dilated just beyond the valves.	(ii) Hosp. p.m. 73. Considerable wasting.	(i) 4 May 1903 (ii) 6 May 1903

41	J.S. 142/03	M	41	Columnar-celled carcinoma of ascending colon	Mesenteric lymph-glands.	General peritonitis.	(ii) Hosp. p.m. 109. Slight wasting.	(i) 10 June 1903 (ii) 24 June 1903 (iv) Resection of colon
42	E.F. 179/03	M	51	Columnar-celled carcinoma of ascending colon	None.	General peritonitis.	(ii) Hosp. p.m. 139. Well nourished.	(i) 17 July 1903 (ii) 26 July 1903 (iv) Resection of colon
43	W.P. 139/03	M	55	Columnar-celled carcinoma of splenic flexure.	None.	Perforation of cæcum. Purulent peritonitis. Polypi of large intestine.	(ii) Hosp. p.m. 102.	(i) 8 June 1903 (ii) 14 June 1903
44	G.W. 136/03	M	53	Columnar-celled carcinoma of sigmoid.	Liver.*	*Lungs:* numerous caseous foci and consolidation in right lower lobe.	(ii) Hosp. p.m. 100. Great wasting.	(i) 21 April 1903 (ii) 13 June 1903
45	R.T. 103/03	M	59	Columnar-celled carcinoma of sigmoid flexure of colon.	Lumbar lymph-glands, liver.	*Lungs:* cicatrization at both apices. Bronchial lymph-glands, caseous and calcareous.	(ii) Hosp. p.m. 74. Body well nourished.	(i) 1 May 1903 (ii) 6 May 1903 (iv) Inguinal colotomy
46	J.E. 64/03	M	54	Spheroidal-celled carcinoma of rectum.	None.	General peritonitis. Atonic distension of large intestine.	(ii) Hosp. p.m. 52. Body well nourished.	(i) 21 March 1903 (ii) 31 March 1903 (iv) Excision of rectum
47	H.P. 167/03	M	56	Columnar-celled carcinoma of rectum, invading bladder; recto-vaginal fistula.	Liver.	.. ..	(ii) Fairly well nourished.	(i) 6 Dec. 1902 (ii) 6 July 1903 (iv) Left inguinal colotomy
48	A.C. 158/03	M	60	Columnar-celled carcinoma of rectum, extending to sacrum.	Liver, right kidney.	*Heart:* aortic cusps slightly atheromatous. Thyroid lateral lobes calcified. Loose smooth fibrous mass in pelvic cavity.	(ii) Marked wasting.	(i) 31 March 1903 (ii) 28 June 1903
49	C.E. 39/03	M	60	Columnar-celled carcinoma of rectum.	Liver.	*Stomach:* polypus 3 cm. in diameter, springing from middle of posterior wall (tubular adenoma).	(ii) Wasting.	(i) 25 Nov. 1902 (ii) 18 Feb. 1903

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50	H.J.C. 63/03	M	62	Columnar-celled carcinoma of rectum (becoming transitional).	Liver.	.. ..	(i) Duodenal pouch. (ii) Great wasting	(i) 25 April 1902 (ii) 25 March 1903 (iv) Left inguinal colotomy
51	E.D. 69A/03	F	29	Columnar-celled carcinoma of rectum.	Left ovary, abdominal wall.	.. ..	(ii) Hosp. p.m. 50. Some wasting.	(i) 10 March 1903 (ii) 30 March 1903 (iv) Excision of rectum
52	E.D. 276/03	F	40	Columnar-celled carcinoma of rectum.	None.	General peritonitis.	(i) Duodenal pouch. (ii) Hosp. p.m. 238.	(i) 23 Nov. 1903 (ii) 12 Dec. 1903 (iv) Excision of rectum
53	M.A.P. 98/03	F	53	Columnar-celled carcinoma of rectum.	Vagina, pelvic and inguinal lymph-glands,* skin.	*Uterus:* multiple fibromata.	(i) Meckel's diverticulum. (ii) Much wasting.	(i) 11 April 1903 (ii) 5 May 1903
54	E.W. 219/03	F	78	Columnar-celled carcinoma of rectum; recto-vaginal fistula.	None.	*Lungs:* chronic bronchitis. *Gall-bladder:* contains calculi.	(ii) Great wasting.	(i) 20 Jan. 1903 (ii) 17 Sept. 1903
55	J.Q. 96/03	M	67	Columnar-celled carcinoma of right lobe of liver.	Right adrenal, portal lymph-gland.	.. ..	(ii) Hosp. p.m. 69. Wasting.	(i) 17 April 1903 (ii) 2 May 1903
56	T.S. 254/03	M	55	Spheroidal-celled carcinoma of gall-bladder, extending into liver and pancreas.	Portal lymph-glands, liver.	*Gall-bladder:* contains a calculus.	(ii) Hosp. p.m. 209. Wasting and jaundice.	(i) 3 Oct. 1903 (ii) 26 Oct. 1903

57	S.W. 289/03	F	61	Columnar-celled carcinoma of gall-bladder (no calculus found), invading liver.	Portal and cœliac lymph-glands, liver.	*Gall-bladder:* contains five calculi.	(ii) Hosp. p.m. 243. Body well nourished. Jaundice.	(i) 5 Dec. 1903 (ii) 22 Dec. 1903
58	W.R. 268/03	M	60	Columnar-celled carcinoma of pancreas (head end chiefly).	Bile duct.	Great hæmorrhagic effusions in peritoneal cavity, pleura, and bladder.	(ii) Hosp. p.m. 218. Body well nourished. Jaundice.	(i) 31 Oct. 1903 (ii) 13 Nov. 1903 (iv) Exploratory laparotomy
59	C.S. 265/03	F	68	Columnar-celled carcinoma of head of pancreas.	Portal lymph-glands, lung, ovary.	*Lungs:* pneumonia right lower lobe. *Pancreas:* duct dilated.	(ii) Hosp. p.m. 216. Body well nourished.	(i) 27 Oct. 1903 (ii) 12 Nov. 1903 (iv) Cholecystotomy
60	S.S. 230/03	M	47	Spheroidal-celled carcinoma of left adrenal, extending to kidney.	Prevertebral lymph-glands, vertebræ.	*Lungs:* hypostatic pneumonia.	(ii) Hosp. p.m. 194. Great wasting.	(i) 26 Sept. 1903 (ii) 28 Sept. 1903
61	H.C. 210/03	M	52	Transitional-celled carcinoma of left ureter, middle part, invading iliacus muscle and extending also to pelvis of kidney.	Abdominal lymph-glands.	Perforation of left ureter. Purulent peritonitis. Right kidney, lower portion fibroid; ureter dilated. *Lungs:* cicatrization at both apices.	(ii) Hosp. p.m. 178.	(i) 27 Aug. 1903 (ii) 5 Sept. 1903
62	P.P. 161/03	M	46	Squamous-celled carcinoma of bladder (no cell nests), extending to prostate.	Liver, portal lymph-glands.	.. ..	(ii) Hosp. p.m. 149. Slight wasting.	(i) 26 June 1903 (ii) 4 Aug. 1903 (iv) Recent cystotomy
63	J.W. 35/03	M	48	Carcinoma of bladder (usual type), infiltrating rectum.	None.	*Kidneys:* hydronephrosis left side.	(ii) Hosp. p.m. 26. Wasting.	(i) 2 Oct. 1902 (ii) 12 Feb. 1903
64	C.P. 145/03	F	44	Squamous-celled carcinoma of neck of bladder (no cell nests).	None.	.. ..	(ii) Fairly well nourished.	(i) 5 Feb. 1903 (ii) 20 June 1903
65	S.W. 107/03	F	64	Squamous-celled carcinoma of urethra, invading bladder (no cell nests).	Pelvic lymph-glands, right lung.	*Kidneys:* double hydronephrosis.	(ii) Body well nourished.	(i) 25 March 1903 (ii) 9 May 1903

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66	S.N. 163/03	F	43	Spheroidal-celled carcinoma of uterus (corpus).	Lumbar lymph-glands, pancreas, left kidney, left adrenal, duodenum, second and third lumbar vertebræ.	Pericardium adherent. *Kidneys:* double hydronephrosis.	(ii) Some wasting. Œdema of feet.	(i) 15 June 1903 (ii) 3 July 1903 (iv) Pan-hysterectomy.
67	M.R. 272/03	F	63	Spheroidal-celled carcinoma of uterus (corpus), involving ovaries and Fallopian tubes.	Prevertebral lymph-glands, wall of jejunum.	.. ..	(ii) Hosp. p.m. 224. Slight wasting.	(i) 1 Oct. 1903 (ii) 18 Nov. 1903
68	A.M.D. 206/03	F	35	Squamous-celled carcinoma of uterus (cervix), extending to bladder.	Left ovary, pelvic and lumbar lymph-glands.*	*Lungs:* inhalation pneumonia. *Kidneys:* slight hydronephrosis on both sides. Peritoneal adhesions. Cyst-like cavities (broken-down growth) in right psoas and under left obturator fascia.	(ii) Wasting.	(i) 13 Aug. 1903 (ii) 2 Sept. 1903
69	R.L. 151/03	F	38	Squamous-celled carcinoma of uterus (cervix).	Pelvic lymph-gland.	*Kidneys:* chronic fibrosis. *Peritoneum:* soft adhesions.	(ii) Wasting.	(i) 6 March 1903 (ii) 24 June 1903
70	S.D. 9/03	F	39	Squamous-celled carcinoma of uterus (cervix), vesico-vaginal fistula.	.. .. ..	*Heart:* vegetations on aortic valves. *Ovaries:* atrophied.	(i) *Liver:* peculiar lobulation. (ii) Body well nourished.	(i) 9 Dec. 1902 (ii) 15 Jan. 1903
71	E.C.H. 14/03	F	40	Squamous-celled carcinoma of uterus (cervix).	Pelvic lymph-glands, ? ovaries.*	.. ..	(ii) Wasting.	(i) 27 Oct. 1902 (ii) 19 Jan. 1903
72	M.K. 261/03	F	40	Squamous-celled carcinoma of uterus (cervix), extending into corpus, vagina, vulva, broad ligaments, psoas, and iliacus; vesico-vaginal fistula.	Abdominal and pelvic lymph-glands, left lung, thoracic duct.	.. ..	(ii) Some wasting.	(i) 8 June 1903 (ii) 7 Nov. 1903

73	F.T. 48/03	F	42	Squamous-celled carcinoma of uterus (cervix); no cell nests	Left iliac and inguinal lymph-glands.	*Kidneys:* hydronephrosis right side, consecutive nephritis left.	(iii) Great wasting.	(i) 16 Feb. 1903 (iii) 4 March 1903
74	S.P. 238/03	F	42	Squamous-celled carcinoma of uterus (cervix, right side); no cell nests.	Right iliac lymph-glands.	*Heart:* shews fatty degeneration *Gall-bladder:* contains a single calculus.	(ii) Body well nourished.	(i) 4 Sept. 1903 (iii) 12 Oct. 1903
75	M.A.R. 56/03	F	46	Sections lost—uterus (cervix), vesico-vaginal fistula.	? Lumbar lymph-glands.	*Lungs:* cicatrices and caseation at each apex. *Kidneys:* bilateral hydronephrosis.	(ii) Marked wasting; bedsore.	(i) 17 Sept. 1902 (iii) 7 Jan. 1903
76	S.R. 32/03	F	48	Squamous-celled carcinoma of uterus (cervix).	None.	*Lungs:* slight cicatrization at each apex. *Heart:* vegetations on aortic valves. *Kidneys:* hydronephrosis left side.	(ii) Wasting.	(i) 1 Oct. 1902 (iii) 9 Feb. 1903
77	E.C. 220/03	F	48	Squamous-celled carcinoma of uterus (cervix), extending to body of uterus, vagina, vulva, bladder, and urethra; vesico-vaginal fistula.	None.	*Kidneys:* hydronephrosis on left side. Peritoneal adhesions and thickening.	(ii) Some wasting.	(i) 26 Aug. 1903 (iii) 16 Sept. 1903
78	T.A.B. 280/03	F	48	Squamous-celled carcinoma of uterus (cervix); no cell nests. Recurrence in vaginal wall after removal of uterus, extending to bladder.	Iliac lymph-glands.	*Brain:* villous growth (not a secondary deposit), springing from roof of 4th ventricle (sudden death).	(ii) No evidence of wasting.	(i) 27 Nov. 1903 (iii) 7 Dec. 1903 (iv) Abdominal hysterectomy
79	E.P. 75/03	F	52	Squamous-celled carcinoma of cervix uteri, invading pelvic tissues.	Pelvic and lumbar lymph-glands, peritoneum.	Retro-peritoneal hæmatoma.	(ii) Slight wasting.	(i) 25 Nov. 1902 (iii) 9 April 1903 (iv) Left lumbar colotomy
80	C.B. 152/03	F	53	Squamous-celled carcinoma of uterus (cervix); vesico-vaginal fistula.	None.	Larynx, aryepiglottic folds very œdematous.	(ii) Slight wasting.	(i) 22 May 1903 (iii) 25 June 1903

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81	L.H. 61/03	F	59	Squamous-celled carcinoma of uterus (cervix), extending to pelvic connective tissue, vagina and ovaries.	.. ..	.. ..	(ii) Great wasting.	(i) 4 Feb. 1903 (ii) 23 March 1903 (iv) Left inguinal colotomy
82	J.H. 221/03	F	59	Squamous-celled carcinoma of uterus (cervix), extending to right ovary and left pelvic wall and rectum.	Pelvic, lumbar, and left supra-clavicular lymph-glands.	.. ..	(ii) Some wasting.	(i) 14 July 1903 (ii) 19 Sept. 1903
83	E.N. 7/03	F	60	Squamous-celled carcinoma of uterus (cervix); no cell nests.	Pelvic and lumbar lymph-glands, lungs and liver.	*Lungs:* cicatrization at each apex. Subacute peritonitis.	(ii) Wasting. Some œdema of lower limbs.	(i) 29 Dec. 1202 (ii) 13 Jan. 1903 (iv) Left lumbar colotomy
84	M.A.C. 127/03	F	60	Squamous-celled carcinoma of uterus (cervix); vesico-vaginal fistula.	None.	*Lungs:* slight cicatrization at each apex. *Kidneys:* hydronephrosis right side, consecutive nephritis left, pus in peritoneal cavity.	(ii) Great wasting.	(i) 26 Jan. 1903 (ii) 4 June 1903
85	M.A.W. 138/03	F	60	Squamous-celled carcinoma of uterus (cervix); vesico-vaginal fistula.	Pelvic lymph-gland.	*Kidneys:* double hydronephrosis.	(ii) Wasting.	(i) 5 Jan. 1903 (ii) 15 June 1903
86	E.A.S. 114/03	F	70	Squamous-celled carcinoma of uterus (cervix); vesico-vaginal fistula.	Pelvic lymph-gland, liver, ovaries,* left adrenal,* bladder.*	*Lungs:* small calcareous focus lower lobe of right lung. *Gall-bladder:* contains 2 calculi. *Kidneys:* hydronephrosis left side. Great atheroma of descending aorta, splenic and superior mesenteric arteries.	(ii) No wasting.	(i) 12 Aug. 1902 (ii) 20 May 1903

87	A.E.D. 44/03	F	42	Columnar-celled carcinoma of uterus (cervix).	None.	.. ..	(ii) Extreme wasting. Œdema of left leg	(i) 4 Dec. 1902 (ii) 1 March 1903
88	K.H. 278/03	F	43	Columnar-celled carcinoma of uterus (cervix), extending to broad ligaments	Lumbar lymph-glands, left ovary and Fallopian tube Peritoneum and omentum.	Lymphatic varices in left inguinal region. *Lungs:* infarcts. *Heart:* stenosis of mitral valve with recent vegetations. *Gall-bladder:* contains pigment concretions. *Spleen:* infarcted. *Kidneys:* hydronephrosis on both sides.	(ii) Some wasting. Œdema of lower limbs.	(i) 19 Oct. 1903 (ii) 30 Nov. 1903
89	M.A.C. 194/03	F	34	Squamous-celled carcinoma of anterior wall of vagina, invading cervix and bladder.	Right and left iliac lymph-glands.	*Lungs:* calcareous nodule in right middle lobe. *Kidneys:* hydronephrosis on left side. Adenoma of thyroid gland.	(ii) Some wasting.	(i) 7 May 1903 (ii) 13 Aug. 1903
90	M.R. 3/03	F	57	Sections lost—vagina; recto-vaginal fistula.	None.	*Kidneys:* chronic fibrosis. *Uterus:* interstitial myoma.	(ii) Fairly well nourished. Œdema of legs and feet.	(i) 7 Feb. 1902 (ii) 4 Jan. 1903
91	S.H. 128/03	F	67	Squamous-celled carcinoma of vagina (anterior wall); vesico-vaginal fistula.	.. .. ..	*Lungs:* slight cicatrization left apex. *Uterus:* small fibromyomata. Phleboliths in broad ligament plexuses.	(ii) Wasting.	(i) 2 Feb. 1903 (ii) 5 June 1903
92	E.W. 4/03	F	59	Squamous-celled carcinoma of vulva.	Right inguinal lymph-glands and one left femoral.*	*Lungs:* bronchiectasis of lower lobes, cicatrices, and calcified foci at each apex.	(ii) Wasting. Œdema of feet.	(i) 20 June 1902 (ii) 3 Jan. 1903
93	A.W. 13/03	F	34	Spheroidal-celled carcinoma of left breast.	Right breast,* left axillary and cervical lymph-glands, lungs,* liver, adrenals, lumbar vertebræ, mandible.	*Lungs:* slight cicatrization at left apex.	(ii) Great wasting.	(i) 18 Oct. 1902 (ii) 19 Jan. 1903

No.	Cancer Register Number.	Sex	Age at death.	Nature of new growth and part primarily affected.	Secondary formations of new growth.	Morbid changes present other than those apparently due to new growth.	(i) Congenital abnormalities. (ii) General remarks.	(i) Date of admission. (ii) Date of death. (iii) Duration of disease on admission. (iv) Surgical operation, if any.
94	E.C. 222/03	F	36	Spheroidal-celled carcinoma of right breast, extending to muscles and pleura.	Axillary and supra-clavicular lymph-glands,* both ovaries, round ligament of liver.*	.. ..	(ii) Body well nourished.	(i) 19 Sept. 1903 (ii) 21 Sept. 1903
95	S.A. 26/03	F	37	Spheroidal-celled carcinoma of left breast.	Lumbar lymph-glands, pleura, lumbar vertebra.*	*Heart:* fatty.	(ii) Wasting.	(i) 29 Dec. 1902 (ii) 3 Feb. 1903
96	E.R. 279/03	F	39	Spheroidal-celled carcinoma of right breast.	Right axillary lymph-glands, lungs, left ovary, pleuræ, pericardium.	.. ..	(ii) Some wasting.	(i) 27 June 1903 (ii) 4 Dec. 1903
97	S.B. 59/03	F	43	Spheroidal-celled carcinoma of both breasts.	Bronchial lymph-gland, lung, cerebrum, cerebellum.	*Lungs:* in left lower lobe is a vomica (? tuberculosis.)	(ii) Hosp. p.m. 44. Body well nourished.	(i) Feb. 1903 (ii) 17 March 1903
98	M.B. 79/03	F	43	Spheroidal-celled carcinoma of breast.	Clavicle.	.. ..	(ii) Notes unfortunately lost.	(ii) April 1903
99	G.G. 264/03	F	44	Spheroidal-celled carcinoma of right breast.	Left breast,* left mediastinal and axillary lymph-glands* both sides, lung, pleura, thyroid gland, stomach, clavicle, pericardium, sternum.	*Kidneys:* hydronephrosis on both sides. *Uterus:* fibromyomata. Left clavicle fractured and seat of growth.	(ii) Wasting.	(i) 20 Dec. 1902 (ii) 11 Nov. 1903 (iv) Amputation of right breast
100	H.S.H. 182/03	F	45	Spheroidal-celled carcinoma of right breast.	Right and left pleura.	*Pleura:* effusion of blood-stained fluid on both sides.	(ii) Body well nourished.	(i) 23 June 1903 (ii) 31 July 1903

101	L.W. 266·03	F	45	Spheroidal-celled carcinoma of right breast, extending to pleura.	Axillary lymph-glands, lungs, liver, vertebræ (thoracic).	*Intestine:* small polypus in small intestine. *Uterus:* erosion of cervix.	(ii) Body well nourished.	(i) 27 Oct. 1903 (ii) 6 Nov. 1903
102	M.B. 287·03	F	47	Spheroidal-celled carcinoma of right breast.	Right axillary lymph-glands, liver, ovaries, vertebra.	.. ..	(ii) Great œdema of right upper limb. Slight wasting.	(i) 15 June 1903 (ii) 22 Dec. 1903
103	C.S. 81·03	F	49	Spheroidal-celled carcinoma of left breast.	Cervical, clavicular, axillary, sternal lymph-glands, skin of breast, pleura, adrenals, pericardium.	.. ..	(ii) Great wasting. Pigmentation. Œdema of left arm.	(i) 6 Sept. 1902 (ii) 21 April 1903
104	N.O. 110·03	F	53	Spheroidal-celled carcinoma of left breast.	Left axilla, mesenteric lymph-glands, skin, left pleura, liver, pancreas,* left adrenal, lumbar vertebra.*	*Lungs:* cicatrization at right apex.	(ii) Wasting. Great œdema of left arm.	(i) 10 May 1903 (ii) 14 May 1903
105	J.S. 274·03	F	59	Spheroidal-celled carcinoma of right breast.	Axillary and pelvic lymph-gland, liver, lung.	*Uterus:* sub-peritoneal and interstitial fibromyomata.	(ii) Hosp. p.m. 228. Body well nourished.	(i) 18 Nov. 1903 (ii) 24 Nov. 1903
106	S.A.T. 74·03	F	60	Spheroidal-celled carcinoma of left breast.	Axillary and tracheal lymph-glands, lungs, pleura and pericardium, skin.	.. ..	(ii) Great wasting and pigmentation.	(i) 6 June 1901 (ii) 8 April 1903
107	E.T. 253·03	F	61	Spheroidal-celled carcinoma of left breast.	Supra-clavicular lymph-glands, lung, adrenals, pericardium, pleura, peritoneum and omentum, lumbar vertebræ.	*Stomach:* stellate cicatrix in middle of greater curvature. *Pleura:* effusion into left cavity.	(ii) Body well nourished.	(i) 2 July 1903 (ii) 26 Oct. 1903 (iv) Amputation of left breast

No.	Cancer Register Number.	Sex.	Age at death.	Nature of new growth and part primarily affected.	Secondary formations of new growth.	Morbid changes present other than those apparently due to new growth.	(i) Congenital abnormalities. (ii) General remarks.	(i) Date of admission. (ii) Date of death. (iii) Duration of disease on admission. (ii) Surgical operation, if any.
108	S.P. 22/03	F	69	Spheroidal-celled carcinoma of right breast.	Right axillary lymph-gland and subcutaneous tissue, mesenteric lymph-glands, lungs,* liver,* pleura, pancreas,* rib, pericardium, kidney (left), adrenals.	.. ..	(ii) Body is wasted.	(i) 20 Dec. 1902 (ii) 29 Jan. 1903
109	R.D. 68/03	M	60	Squamous-celled carcinoma of right thigh.	Right femoral lymph-glands.	.. ..	(ii) Wasting.	(i) 29 Sept. 1902 (ii) 28 March 1903
110	R.D. 30/03	F	9	Proliferating cyst-adenoma of kidney (histological appearances determined from secondary growths in liver and gland: the renal growth has rather the appearances of a transitional-celled carcinoma).	Left kidney, liver, pancreas, omentum, lumbar lymph-gland.	.. ..	(ii) Hosp. p.m. 22. Wasting.	(i) 29 Jan. 1902 (ii) 8 Feb. 1903
111	W.C. 243/03	M	60	Proliferating cyst-adenoma of the left kidney.	None.	*Heart:* aortic incompetence. *Bladder:* inflamed. *Kidneys:* bilateral suppurative pyelitis. *Duodenum:* adenomatous condition of Brunner's glands.	(ii) Hosp. p.m. Body thin.	(i) 3 Oct 1903 (ii) 16 Oct. 1903

SARCOMATA.

No	Cancer Register Number.	Sex.	Age at death.	Nature of new growth and part primarily affected.	Secondary formations of new growth.	Morbid changes present other than those apparently due to new growth.	(i) Congenital abnormalities. (ii) General remarks.	(i) Date of admission. (ii) Date of death. (iii) Duration of disease on admission. (iv) Surgical operation, if any.
1	G B. 286 03	M	51	Mixed-celled sarcoma of right cervical lymph-glands, extending over right scapula.	Left cervical and axillary lymph-glands, left pleura and lung.	*Brain*: both lateral ventricles distended, with fluid; psammomata. *Heart*: slight aortic incompetence.	.. .. ..	(i) 16 Oct. 1903 (ii) 20 Dec. 1903
2	E.H. 250 03	M	60	Mixed-celled sarcoma of middle of stomach.	Cœliac lymph-glands, omentum, peritoneum.	*Lungs*: slight cicatrization at each apex. *Peritoneum*: contains 5 pints of clear fluid.	(i) Meckel's diverticulum. (ii) Great wasting.	(i) 15 June 1903 (ii) 24 Oct. 1903
3	R.M. 148 03	F	20	Mixed-celled sarcoma of neck (? left tonsil), both sides.	Cervical, supra-clavicular, omental, mediastinal, and lumbar lymph-glands, pleura, larynx,* peritoneum.*	*Larynx*: œdema of ary-epiglottic folds. *Lungs*: right completely collapsed, left partially so.	(i) Body well nourished.	(i) 19 Feb. 1903 (ii) 21 June 1903
4	E.C. 234 03	F	38	Mixed-celled sarcoma of nasal cavity, involving body and greater wing of sphenoid.	.. .. ..	Small partially calcified adenoma of thyroid. *Lungs*: slight cicatrization at each apex.	(ii) Extreme wasting.	(i) 4 July 1903 (ii) 3 Oct. 1903
5	E.B. 129 03	F	63	Mixed-celled sarcoma of nasal cavity, invading ethmoid bone.	.. .. ..	*Lungs*: cicatrices at each apex. *Gall-bladder*: 27 calculi. Phleboliths in venous plexuses.	(ii) Some wasting.	(i) 26 May 1903 (ii) 5 June 1903
6	J.H. 120 03	M	20	Small round-celled sarcoma of left antrum, destroying olfactory lobes.	Tentorium cerebelli, sternal lymph-gland.	*Larynx*: right half œdematous.	(ii) No wasting.	(i) 30 March 1903 (ii) 27 May 1903
7	J.P. 160 03	M	38	Small round-celled sarcoma of pyloric end of stomach.	None.	Peritonitis.	(ii) Hosp. p.m. 114. Some wasting.	(i) 18 June 1903 (ii) 29 June 1903 (iv) Gastro-jejunostomy

No.	Cancer Register Number.	Sex.	Age at death.	Nature of new growth and part primarily affected.	Secondary formations of new growth.	Morbid changes present other than those apparently due to new growth.	(i) Congenital abnormalities. (ii) General remarks.	(i) Date of admission. (ii) Date of death. (iii) Duration of disease on admission. (iv) Surgical operation, if any.
8	A.J. 173/03	M	38	Round-celled sarcoma of left kidney.	Liver, spleen, peritoneum.	*Lungs:* slight cicatrization at left apex. *Intestines:* a few ulcers about 8 inches above ileocæcal valve. Chronic inflammatory thickening of abdominal connective tissues.	(ii) Marked wasting.	(i) 25 Feb. 1903 (ii) 15 July 1903
9	J.S. 201/03	M	38	Small round-celled sarcoma of larynx.	Pyloric end of stomach, submaxillary lymph-glands.*	.. ..	(ii) Hosp. p.m. 172. No wasting.	(i) 1 Aug. 1903 (ii) 28 Aug. 1903
10	J.P. 100/03	M	70	Small round-celled sarcoma of thyroid cartilage.	.. .. ..	*Lungs:* broncho-pneumonia.	(ii) Hosp. p.m. 58. Some wasting.	(i) 16 April 1903 (ii) 6 May 1903
11	E.C. 1/03	F	$\frac{5}{12}$	Small round-celled sarcoma of right orbit and frontal bone.	Left orbit, kidneys, stomach, left femur.	.. ..	(ii) Hosp. p.m. 1.	(i) 31 Dec. 1902 (ii) 1 Jan. 1903
12	S.R. 86/03	F	33	Small round-celled sarcoma of stomach.	Abdominal lymph-glands,* pancreas.	.. ..	(ii) Hosp. p.m. 63. Great wasting.	(i) 10 Feb. 1903 (ii) 27 April 1903
13	E.P. 137/03	F	32	Sarcoma of frontal bone (? osteo-sarcoma), right side.	None.	Purulent meningitis.	.. .. ..	(i) 20 April 1903 (ii) 13 June 1903 (iv) Removal of portion of growth
14	L.K. 159/03	F	53	Spindle-celled sarcoma of left ovary.	None.	Thrombosis of left iliac and right femoral veins.	(ii) Hosp. p.m. 111. Œdema of lower extremities. Wasting.	(i) 9 March 1903 (ii) 26 June 1903
15	G.G. 273/03	M	44	Lympho-sarcoma of mediastinal lymph-glands, invading pleura, pericardium, and pulmonary vein.	Lung, bronchial lymph-glands, liver.	.. ..	(ii) Hosp. p.m. 225. Slight wasting.	(i) 10 Nov. 1903 (ii) 22 Nov. 1903

16	W.E. 281/03	M	64	Lympho-sarcoma of mediastinal lymph-glands, extending into lung along left bronchus.	Cœliac lymph-glands, liver, lungs.	.. ..	(ii) Hosp. p.m. 235. Considerable wasting.	(i) 17 Nov. 1903 (ii) 7 Dec. 1903
17	J.R. 189/03	F	18	Lympho-sarcoma of cervical lymph-glands left side, invading thyroid body.	Bronchial lymph-glands, lungs.	.. ..	(ii) Some wasting.	(i) 16 June 1903 (ii) 10 Aug. 1903
18	E.P. 99/03	F	19	Lympho-sarcoma of neck (left side).	Mediastinal, axillary, and mesenteric lymph-glands, liver* (?), sacrum.*	.. ..	(ii) Hosp. p.m. 72. Marked wasting.	(i) 17 March 1903 (ii) 6 May 1903
19	E.M. 184/03	F	56	Lympho-sarcoma of mediastinal glands, invading right lung.	Cervical lymph-glands, pericardium, liver, pancreas.	*Lungs:* bronchiectasis on right side. Cicatrization at left apex.	(ii) Hosp. p.m. 145. Wasting.	(i) 19 May 1903 (ii) 1 Aug. 1903
20	E.R. 76/03	F	60	Lympho-sarcoma of mediastinum.	Right kidney and adrenal, pericardium, heart.	.. ..	(ii) Hosp. p.m. 55. Wasting.	(i) 24 Feb. 1903 (ii) 10 April 1903 (iv) Removal of subcutaneous nodule, for diagnosis
21	H.C. 252/03	M	42	Endothelioma of anterior portion of tongue (lymphatic type).	Lymph-glands, liver.	Five short stalked polypi in colon.	(i) Duodenal pouch. (ii) Body well nourished.	(i) 5 Oct. 1903 (ii) 25 Oct. 1903
22	J.R.J. 57/03	M	45	Endothelioma (lymphatic type) of right external auditory meatus, invading tympanum.	Right cervical lymph-glands, lungs, pericardium.	.. ..	(i) Meckel's diverticulum. (ii) Great wasting.	(i) 26 Nov. 1902 (ii) 15 March 1903
23	T.T. 67/03	M	64	Endothelioma of tongue, extending to right tonsil (lymphatic type).	Cervical lymph-glands.	.. ..	(ii) Great wasting.	(i) 8 Oct. 1902 (ii) 27 March 1903

No.	Cancer Register Number.	Sex.	Age at death.	Nature of new growth and part primarily affected.	Secondary formations of new growth.	Morbid changes present other than those apparently due to new growth.	(i) Congenital abnormalities. (ii) General remarks.	(i) Date of admission. (ii) Date of death. (iii) Duration of disease on admission. (iv) Surgical operation, if any.
24	W.G. 43/03	M	49	Endothelioma of tongue, left margin (hæmal type). Tongue œdematous anteriorly.	Cervical lymph-glands, lungs.	Omental hernia (left inguinal).	(i) Meckel's diverticulum. (ii) Considerable wasting.	(i) 26 Nov. 1902 (ii) 25 Feb. 1903
25	M.R. 69/03	F	29	Endothelioma (lymphatic type) of right middle ear, extending into right temporal bone.	Lungs.	.. ..	(i) Episternal bones (large). (ii) Body well nourished.	(i) 26 April 1902 (ii) 29 March 1903
26	C.E.C. 239/03	F	57	Endothelioma (lymphatic type) of left breast, infiltrating entire thickness of chest wall.	Bronchial lymph-glands. Ampulla of Vater, stomach, left kidney, thyroid body, peritoneum, pericardium.	*Common bile duct:* dilated. *Uterus:* several small fibromyomata. *Pleura:* effusion into left cavity.	(ii) Slight wasting. Marked jaundice. Great œdema of left arm and hand. "Cancer en cuirasse" of left breast.	(i) 9 Jan. 1903 (ii) 10 Oct. 1903

THE CENTRIFUGAL SPREAD OF MAMMARY CARCINOMA IN THE PARIETES AND ITS BEARINGS ON OPERATIVE TREATMENT.

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I.—INTRODUCTION.

In the following Paper it is proposed to consider chiefly from the clinical and macroscopical standpoint certain facts in the Pathology of Breast Cancer which hardly seem to have obtained due recognition. At the same time such modifications in operative procedure as are deducible from the pathological facts will be briefly indicated.

The necessity of scrupulously clearing out from the axilla every particle of its fat, connective tissue, and glands is so generally accepted that there is no necessity to consider this branch of the subject. Stiles has shewn that the whole breast must be removed, and that, in order to do this, the pectoral fascia and the costal part of the great pectoral muscle must be taken away. In America there is a tendency at present to extend the area of operation upwards, and to remove the glands of the posterior triangle as a matter of routine, a practice which most English surgeons regard as unnecessary.

Although the scope of the operation has been thus widened, recognition still seems to be denied (at any rate in practice) to the fact that the axillary and supra-clavicular glands, and the lymphatic routes which lead to them, are by no means the only extra-mammary structures to which comparatively early extension of the growth occurs.

There is much evidence that cancer of the breast spreads centrifugally and by continuity from its seat of origin in a way not unlike the spread of erysipelas, though not in the same plane. The area of extension in both instances is rather bounded by two dimensions than by three, and tends to assume a circular form, with the primary focus as centre. Thus, erysipelas spreads essentially in the plane of the skin, and carcinoma often shews a tendency to spread widely in the plane of the parietes, before involving the internal viscera.

Leaving aside the embolic infection of the axillary glands, the infected area of the parietes as the growth advances might be represented roughly by circles of ever increasing radius centred on the primary growth. In some cases centrifugal extension may ultimately involve the greater part of the surface of the body. It appears to take place quite independently of any transport of cancer particles by the blood or lymph streams, and rather proceeds by direct growth along the finer lymph vessels.

II.—CENTRIFUGAL EXTENSION IN THE PARIETES.

There are five layers in which evidence of the centrifugal extension of mammary cancer may be sought. These are—

(i) The skin.
(ii) The subcutaneous fat.
(iii) The deep fascia.
(iv) The muscles.
(v) The bones.

Since, however, subcutaneous nodules affect both the skin and the subcutaneous fat at the same time, and since little is known of cancer in muscle, the layers to be considered are practically reduced to three—

(i) The skin and subcutaneous fat.
(ii) The deep fascia.
(iii) The bones.

The secondary deposits in each of these layers must now be considered separately with regard to the question of centrifugal spread.

(i) The Skin and Subcutaneous Fat.

It is almost an axiom in the present day pathology of breast cancer that the skin is early infected, and that cancer extends along it in all directions from the primary growth. The subcutaneous nodules which so frequently appear in the neighbourhood, and later involve a very wide area round it, are often regarded as conclusive evidence on this point. Discussion of this view may for the present be deferred.

Careful observations on the appearance and spread of skin-nodules are hard to find. It seems, however, quite certain that these nodules always appear first in the immediate neighbourhood of the primary growth. They are very rarely found on the scalp, the upper arm, or the abdomen until some time after they have made their appearance on the front of the chest.

Stanley Boyd,* in a paper on Oöphorectomy for Breast Cancer, gives three very careful sketches of the same case at different periods. The centrifugal extension of the area in which skin-nodules occur is clearly manifested. The growth was in the right breast. At first about five subcutaneous nodules were seen on the affected side of the front of the chest, near the operation scar. Next a nodule appeared at the anterior edge of the right latissimus dorsi. Later, nodules appeared in the right upper arm, at the right scapular angle, over the left side of the front of the chest, and in the skin of the abdomen over the epigastric angle. In a late stage the nodules became so numerous over the front of the abdomen nearly down to the pubes that it was impossible to chart them.

The following two cases from the records of The Middlesex Hospital also illustrate the spread of subcutaneous nodules in the region surrounding the primary growth.

In the first case the left breast presented a surface which was raised and ulcerated in part, and the skin around was nodular from the existence of numerous subcutaneous deposits of new growth, which extended over the front of the left half of the chest in its upper part, and also over and about the right clavicle. In a backward direction these deposits could be

* "On Oöphorectomy in the Treatment of Cancer of the Breast," Boyd. ("British Medical Journal," February 4th, 1899, p. 257.)

detected nearly to the posterior axillary fold. The left shoulder was covered by this subcutaneous nodulated growth, and was almost fixed. (P.M. Register, 1901, No. 59.)

The other case shewed a wider distribution of skin nodules, but nevertheless the distal portions of the limbs were free. There was great wasting, and the body presented a remarkable appearance owing to numerous large (1—2 inches diameter) secondary growths in the skin. These growths occurred principally on the front of the chest and abdomen, but were also present on the back, the face, behind the jaw, the eyelids, and the limbs. In the latter situation it is especially noted that the chief distribution was on the parts near the trunk.

Many of the nodules on the chest were ulcerated; others were rounded and projected for nearly an inch. A large growth was situated over the sternum, and thence indefinite lines of nodules seemed to radiate in all directions. About an inch to the right side of the linea alba, and parallel to it, was a conspicuous line of nodules. In most instances the nodules were subcutaneous, and did not extend to the deeper layers of the parietes. No deposits were found in the lungs. (P.M. Register, 1902, No. 52.)

The most extreme instance of widely disseminated skin-nodules I have found is one recorded by Rolleston.* The primary growth was a small one in the lower and outer part of the left breast, and the breast was removed, along with two glands in the left axilla, which were found to be carcinomatous. Twenty-one months after the operation a small nodule was noticed under the skin over the right clavicle. Subsequently very numerous nodules developed. A year after the first recurrence there were 105 of these, together with a mass in the right mamma. Four months later, simultaneously with the administration of arsenic and thyroid extract, the number of nodules had diminished to 78. The glands in the axillæ and groins were enlarged.

The distribution of the nodules is illustrated in two figures, one shewing the front, the other the back of the body. The figures afford very strong evidence for centrifugal spread, in

* "A Case of Multiple Cutaneous Carcinomatosis after Carcinoma Mammæ," by H. D. Rolleston, M.D. (Clinical Society's Transactions, vol. xxxiv., 1901, p. 206.)

that *the arms below the middle of the humerus, and the lower limbs below the upper third of the femur, are entirely free from nodules.* In Dr. Rolleston's opinion the nodules had become disseminated by the blood stream, but such a hypothesis seems quite inconsistent with the entire escape of the distal extremities of the body, the regions where the circulation is terminal, and where non-cancerous embolism at all events produces its most characteristic effects.

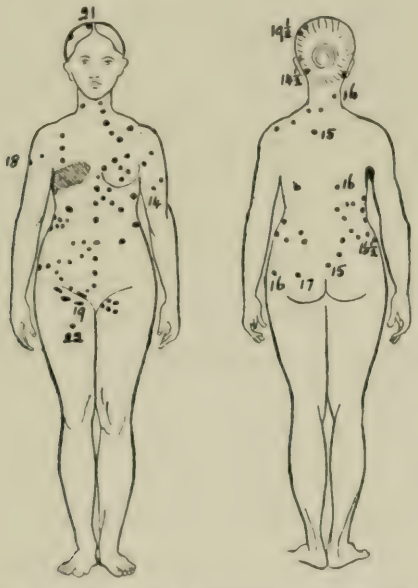

FIG. 1.—DIAGRAM SHEWING THE DISTRIBUTION OF THE SUBCUTANEOUS NODULES IN DR. ROLLESTON'S CASE.

The *left* breast was previously removed for carcinoma. The shaded area over the right mammary region represents a number of closely-packed secondary growths. The figures attached to certain of the nodules represent their distance in inches from the left nipple, measured by the shortest route along the skin surface.

The writer is indebted to Dr. Rolleston for permission to use this diagram.

It is true that there are numerous nodules in the scalp which could be explained by embolism, but the hypothesis is unnecessary. By marking the position of the most remote nodules in Rolleston's diagrams on the skin of a living subject, and taking actual measurements by the shortest route along the skin surface, it was found that the uppermost nodule

i.e., one on the scalp in front, was about 21 inches distant from the situation of the left nipple. The most remote nodule downwards, that in the right groin, was 22 inches from the same point. The nodule furthest to the right, when the right arm was raised, was 18 inches from the left nipple; that furthest to the left, on the left arm, was 14 inches from the left nipple. Many of the nodules on the back, measuring around the thorax either to right or left, were between 15 and 17 inches distant from the left nipple. Indeed, on the posterior aspect of the trunk the edges of the infection circle, serpiginous by reason of the irregularities of the surface, seem clearly traceable, as its opposite convexities wrap round the body and tend to meet towards the right side of the back. The parts of the back most remote from the left nipple are free from nodules. These parts are, of course, the right scapular and the right gluteal regions.

If we assume that a small part of the primary growth was left behind about two inches internal to the left nipple, and just below it, all the nodules fall just within an oval area of 21½ by 16 inches, having this point as centre, and with its long axis vertical. They have spread just as much upwards as downwards, and just as much to the right as to the left. It must, however, be admitted that within the nodule area their distribution is somewhat irregular, as is evidenced by the escape of the face and much of the left side of the abdomen. The point, therefore, upon which chief stress must be laid as an indication of centrifugal spread is the absolute immunity of the parts of the body beyond the area indicated, *i.e.*, the distal portions of the limbs.

A recent case at The Middlesex Hospital shewed a similar, but less extensive distribution of subcutaneous nodules, with the same freedom of the limbs from nodules. The distribution is therefore not accidental but characteristic. The limbs escape no doubt simply because the patient dies before the slow centrifugal spread of the growth has time to extend to them.

Cases of the kind just described have usually been explained upon the assumption that the carcinoma extends in the deep cutaneous plexus of lymphatics at the junction of the corium and the subcutaneous tissue. But no satisfactory evidence has yet been brought forward to prove that cancer spreads *along*

the skin. Indeed, the irregular distribution of subcutaneous nodules within a regular area seems to indicate rather that they are accidental efflorescences of growth which is really extending in a deeper plane. It may be that they are simply the index of continuous spread of growth in the deep fascia.

In this connection it is worthy of note that, though Stiles was able to demonstrate cancerous lymphatics in the connective tissue septa which unite subcutaneous nodules to the deep fascia, he has brought forward no microscopic evidence of any continuity of infection *along the skin* between neighbouring nodules.

The fallacy of arguing that because subcutaneous nodules spread centrifugally from the growth, therefore the growth necessarily spreads along the skin, may be illustrated by the annexed diagram.

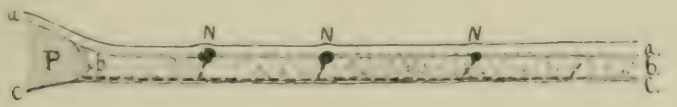

FIG. 2.—To shew that Subcutaneous Nodules do not necessarily imply the extension of growth *along* the skin.

The diagram represents a section of the parietes at right angles to the surface in the region of the primary growth P: a a skin, b b subcutaneous fat, c c deep fascia. The subcutaneous nodules N N N may arise (1) from spread of growth in the skin in the direction of the lightly-dotted line, a view generally held; *or* (2) from spread of growth in the deep fascia, along the heavy interrupted line, with occasional offshoots to the skin, giving rise to subcutaneous nodules. Though this is not the accepted view, it is the correct one in the writer's opinion.

While it is quite possible that the growth spreads along the skin in the direction of the light dotted line, subcutaneous nodules may equally well be explained by extension of the growth in the deep fascia, along the heavy dotted line, with lateral extensions here and there towards the skin.

The question along which of the planes of the parietes breast cancer *primarily* spreads must be deferred until infection of the deep fascia, and of the bones, have been considered.

(ii) The Deep Fascia.

Heidenhain and Stiles have shewn that breast cancer early invades the pectoral fascia, where it is found within the lymphatic vessels which lie on its surface.

The anatomical definition of the expression "pectoral fascia" is the fascia which covers the pectoralis major muscle. Lying in or upon it is a lymphatic network or plexus, giving rise to large vessels which run to the axillary glands. But the lymphatic network is in no way special to the pectoral fascia, nor bounded by its limits. At the margins of the pectoral fascia the plexiform network of lymphatic channels is continued over the abdomen, the opposite pectoral muscle, the neck, and the serratus magnus. In fact, the lymphatic plexus of the deep fascia is found as a continuous network all over the body.

There is, therefore, no anatomical obstacle to prevent cancer from growing along the meshes of the deep fascia over the whole superficial extent of the parietes, along lymphatic vessels which are indeed too small to allow the cells to be carried by the lymph stream, but which must yet offer far less resistance to the growth of cancer along them than is successfully encountered in the infiltration of a solid tissue, by way of its far smaller lymph spaces. That such growth would often have to take place against the direction of the lymph current can hardly be regarded as a valid objection to this view, considering the low intravascular pressure within the small lymphatics, the sluggishness of their stream, and the freedom of their anastomoses.

It may be objected that, if cancer of the breast extended in the fascial lymphatics beyond the limits of the pectoral fascia, its presence would have been detected by so careful an observer as Stiles. It is, therefore, necessary to emphasize the fact that Stiles' work was done exclusively on mammæ excised from the living subject at a time when wide removal of the deep fascia was not practised, so that his material allowed him to trace fascial infection only within narrow limits. Though he could only speak positively of the pectoral fascia, nevertheless, as a measure of precaution, he recommended removal also of the fascia covering the serratus magnus and the upper digitations of the obliquus externus abdominis.

Even, however, up to the present day many surgeons act as though the fascia covering the pectoralis major were the only area of the deep fascia to which mammary carcinoma may extend, and aim only at such a wide removal of it as shall ensure ablation of the whole breast and the mammary lymphatics. But the peripheral lymphatics of the mammary area

themselves anastomose with those of contiguous areas, so that invasion of the deep fascia is almost certainly bounded by a series of ever-widening circles centred on the primary growth—not by the limits of the breast, nor indeed by any anatomical boundaries. The practical importance of such a conclusion is obvious.

That cancer does tend to grow widely along the lymphatic plexuses, and to choke up their meshes, is a well-known fact, though the process has not been definitely recognized in the deep fascia. When cancer cells gain entrance to the pleural or the peritoneal cavity they may implant themselves on the serous surface, and give rise to secondary growths. Around such secondary growths a wide, somewhat opaque, roughly circular area of the serous membrane can often be seen. Close observation reveals the opacity as a fine rete of white lines, just visible to the unaided sight, and shewn microscopically to be due to the growth of cancer along the meshes of the sub-endothelial lymphatic plexus.

It is proposed to publish later a full account of some observations upon this subject.

It is not the object of the present Paper to consider the microscopical evidence for the spread of cancer along the fascial lymphatic plexus. It can, however, be traced to some extent macroscopically by the following method, which has the advantage of rendering visible the coarser ramifications of the growth in the parietes in pieces of some thickness, while the microscope shews only one plane.

1. The tissue to be examined is fixed for a few days in equal parts of commercial formalin and water.
2. A thin slice, vertical to the surface, is cut from it. The slice should not exceed 3—4 mm. in thickness, but may be of any length. Along one edge will be seen the skin, below this the subcutaneous fat, and the subjacent deep fascia and muscle.
3. This slice of tissue is stained for a week in a fluid consisting of nine parts of Müller's fluid to one part of formalin.
4. It is washed in water and transferred to absolute alcohol.
5. When dehydrated it is transferred to cedar-wood oil, and may be preserved in this medium.

The specimen thus obtained should be examined by strong transmitted light. The protoplasmic tissues are stained in various shades of reddish brown, while the fat, which is rendered translucent, remains practically unstained. Cancer in the deep fascia or in muscle stains a reddish brown, while normal muscle stains a darker brown. The method is not suitable for tracing cancer in the skin, which itself is somewhat stained.

Not only are cancer nodules in the fat, fascia, or muscle rendered plainly visible, but the larger cancerous lymphatics are seen as ramifying dark lines. (See Fig. 3.)

(iii) The Bones.

During the thirty years 1872—1901 there have been at The Middlesex Hospital 329 autopsies on cases of mammary carcinoma. Excluding cases where the only bones to which cancer had extended were the sternum or the ribs, there were 37 cases in which the bones were the seat of secondary deposits, or of spontaneous fracture. Including cases where the primary growth had invaded the sternum or the ribs, this total is raised to 73 cases.

The statistics derived from these cases do not afford very reliable information as to the frequency with which different bones are affected by secondary growths.

Speaking generally, post-mortem statistics only afford trustworthy evidence of the frequency of metastases in those bones which are liable to spontaneous fracture. A complete examination of the skeleton is made very rarely indeed, and as a rule the pathologist's attention is not directed to more than the vertebral column unless fractures of the long bones are present.

Since the flat bones may be extensively cancerous without breaking, the escape of the scapula and the pelvic bones from cancerous deposit is almost certainly apparent only. The flat bones of the skull, which usually come under notice during the examination of the brain, are not infrequently found to be the seat of secondary growths, and it would therefore be unsafe to argue that the scapula and the os innominatum are not similarly liable to metastases.

The case of the long bones is different. Whenever a long bone is extensively cancerous, fracture of it is almost certain to occur sooner or later. Not infrequently indeed fractures occur when the body is being actually moved on the post-mortem table. If, therefore, no mention of certain long bones as being either the seat of metastases or fracture is made in the post-mortem records, the presumption in favour of their freedom from extensive new growth is so considerable as almost to amount to a certainty.

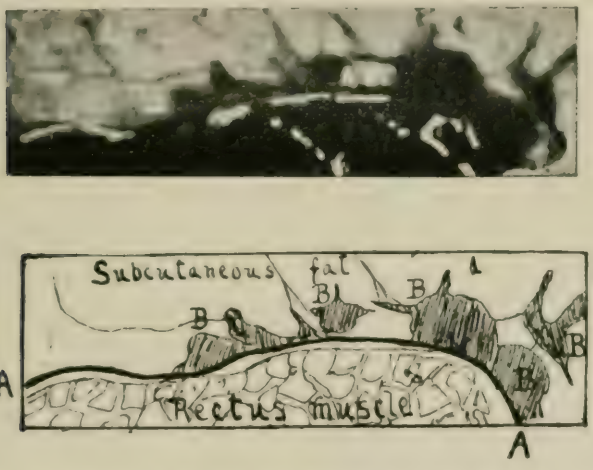

FIG. 3.—Photograph × 3, with key-diagram attached, shews a late stage of cancerous invasion of the deep fascia round a carcinoma of the breast. It represents a horizontal slice of tissue ¼ inch thick taken from the upper part of the abdominal wall. The specimen is viewed by transmitted light. The skin at this level was free from obvious growth, though subcutaneous nodules were present higher up. Above is seen the subcutaneous fat, separated from the rectus muscle by A A, the anterior layer of the rectus sheath. The dark masses marked B are cancer nodules which originated from growth lying within the vessels of the fascial lymphatic plexus. Here and there they are sending prolongations towards the skin.

The specimen was stained and rendered translucent by the method described in this Paper. For the photograph I am indebted to Mr. A. Smith of the Samaritan Hospital.

Spontaneous fractures have been reckoned as indicating metastases at the point of fracture, whether the existence of local growth has been specially mentioned in the records or not.

The following table shews the relative frequency of deposits in the various bones of the skeleton :—

TABLE I.—Shewing the Frequency of Cancerous Deposit or Spontaneous Fracture in 329 Cases of Mammary Cancer at The Middlesex Hospital, 1872—1901.

	Bone.	Number of Cases.	Percentage of Total.
Bones lying wholly or partially within the area liable to subcutaneous nodules.	Sternum	30	9
	Ribs	28	8
	Clavicle	5	1·5
	Spine	12	3·6
	Cranial Bones	9	2·7
	Scapula*	1	·3
	Femur	14	4·2
	Os innominatum*	0	0
	Humerus	9	2·7
Bones lying beyond the area liable to subcutaneous nodules.	Radius	0	0
	Ulna	0	0
	Tibia	1†	·3
	Fibula	0	0
	Patella	1†	·3
	Bones of Hand	1	·3
	Bones of Foot	0	0

Making full allowance for the fallacies inherent in this table, and the errors of omission relating to the bones not liable to spontaneous fracture, it will be found to indicate certain general laws.

(1) *The liability of a Bone to Cancerous Metastasis increases with its proximity to the site of Primary Growth.*

Thus, the sternum and ribs are affected in about the same number of cases, and much more frequently than any of the other bones. The spine, femur, humerus, and cranial bones come next, the clavicle apparently forming an exception to the general rule.

* This bone, owing to its shape, is not much liable to spontaneous fracture, and rarely comes under observation at an autopsy (see p. 36).

† Knee ankylosed, femur affected in its whole length, with extension of growth to patella and head of tibia (see p. 45).

(2) *The Bones distal to the Knee and Elbow escape Cancerous invasion, except in the rarest instances.*

Among the seventy-three cases of bone deposit or fracture there are one real and one apparent exception to this rule. These two cases will be dealt with in detail later on.

If bone deposits take their origin from particles lodging in the peripheral blood-vessels they can best be studied in the limbs, the regions which appear most liable to embolism. If, on the contrary, the view be accepted that bone deposits are incidents in the centrifugal spread of the cancer by continuity, it is equally in the limbs that clear evidence on the point is likely to be obtained. For this reason metastases in the bones of the trunk may be ignored, and attention will be concentrated on the long bones of the limbs.

(*a*) Secondary Deposits in the Femur.

Out of 329 cases there are recorded nine in which one or both femora were the seat of definite deposits, with or without fracture, and five others in which spontaneous fracture alone is said to have occurred. In twelve of the fourteen cases there was fracture of one or both femora; in four cases the fracture was bilateral.

In every case where the deposit was local or the fracture single the pathological condition was present in the upper third of the bone, most often a little (about two inches) below the base of the great trochanter.

This statement is based on eleven of the fourteen cases (see Table III., p. 56), and the apparently exclusive preference of early cancerous growth for this particular part of the bone is a striking fact. The point of election for spontaneous fracture in breast cancer does not coincide with the usual positions of senile fracture of the femur, which is across the neck, nor with the point of entry of the nutrient artery.

There are indications that the base of the great trochanter is the usual point of invasion of the femur, but that, owing to the thickness of the bone at this level, actual fracture generally occurs rather lower down. Thus in Case XII (Table III., p. 58) there was fracture of the right femur "through its upper

third." The new growth was chiefly confined to the upper fragment, involving the great trochanter, *which was largely destroyed*, and the shaft just below.

Again, in Case VII, at the junction of the shaft with the great trochanter, there was a mass of cancer the size of a man's fist. The bone was fractured.

The right femur in Case XI afforded similar evidence. There was new growth over the great trochanter, and again about 3½ inches below this.

Even in cases where the infiltration of the femur is very extensive, or has extended along its whole length, the indications that the bone was originally attacked near the upper end are often quite clear. Thus in Case XIII the right femur was infiltrated in its upper two thirds, the lower third having escaped. In Case III the right femur was distorted and in great part replaced by growth, and only in its lower third was the outline of the bone traceable.

It appears then from this list that secondary cancerous deposit in the femur always commences in the upper third, and never in the distal portion of the bone. There is strong evidence that the great trochanter is the point of first invasion.

(*b*) Secondary Deposits in the Humerus.

Of the 329 cases with which this Paper deals there were six in which one or both humeri were the seat of deposits. In five of these cases attention was directed to the bone by the presence of fracture. In four other cases there was fracture without any definite proof of the presence of growth, making ten in all. In two of these ten cases the fracture was bilateral (see Table IV., p. 59).

Of the eight separate bones in which fracture occurred, and in which the exact site of the break is recorded, it was found just at the middle of the bone in four instances, and through the lower third in the remaining four. Fracture therefore always occurs within the limits of the lower half of the bone, and the seat of election is the mid-point of the bone at the Deltoid insertion.

Cancerous deposit in the humerus is much more frequent than would appear from post-mortem records.

Snow* records eight cases of microscopical infiltration of the bone in an unselected series of twelve cases of cancer of the breast examined by him. The same observer has directed attention to a thickening of the upper epiphysial end of the humerus, sometimes to be felt on the side of the primary growth, which he regards as cancerous.

A cancerous humerus seems to be less liable to spontaneous fracture than the femur, partly because it carries less weight, partly, no doubt, because it is often supported by a firm œdema of the arm, and is also bound to the side by contraction of the axillary growth. Hence post-mortem statistics probably underestimate the frequency of deposit in the humerus, especially as the humerus is liable to a risk not shared by the femur, viz., direct invasion by a mass of axillary growth.

The evidence goes to shew, however, that as a rule it is not direct extension of the axillary growth that leads to spontaneous fracture. *Apparently the humerus is usually invaded at its mid-point—the Deltoid insertion—from which point the growth spreads both upwards and downwards along the medullary canal.* The relative thinness of the lower half of the bone, and the smaller amount of protection it receives, account sufficiently for the incidence of spontaneous fractures on this portion of the bone.

(*c*) Secondary Deposits in Long Bones of the Limbs other than the Humerus and Femur.

These may be very briefly dismissed. In one case the scapula was involved; in another case the head of the tibia was invaded by extension from advanced growth of the femur, apparently by way of an ankylosed knee-joint. In another case there were spontaneous fractures of three metacarpal bones. Both these latter cases will be referred to again.

The absence of records of spontaneous fracture in the distal bones shews that their escape from cancerous invasion is real and not merely apparent.

* "The Insidious Marrow Lesions in Mammary Carcinoma," Snow. ("British Medical Journal," March 12th, 1892, p. 548.)

The Pathogenesis of Bone Metastases.

There is a consensus of opinion that bone metastases in carcinoma mammæ, and in carcinoma generally, are due to transference of particles of the primary growth by way of the blood stream.

A consideration of the evidence seems to shew that the conclusion is an erroneous one, and that, like subcutaneous nodules, bone deposits are secondary results of far-extending growth of cancer along the deep fascial lymphatic plexus. Whether the same holds good for cancer of other regions than the breast is not now the subject of discussion.

These two hypotheses may now be considered separately.

A. *Are bone metastases due to blood-infection?*

(*a*) There is one fact with reference to secondary growths of the femur and humerus which seems at first sight strongly to suggest their origin from emboli carried along the blood-vessels. Bone deposits in an early stage involve the upper third of the femur, but the lower half of the humerus. They thus occur mostly in that district of the bone towards which the nutrient artery of the shaft is directed.

More closely examined, this contention loses much of its force. The seat of election for cancer of the femur is the great trochanter; of the humerus, it is at the Deltoid insertion. One would rather imagine, if the process were embolic, that the seat of election in the femur should be in the neck, near the epiphysial line, and not at a point distinctly lower down. Again, in the humerus, where the nutrient artery enters below the mid-point of the bone, the line at which fracture is most often found—the Deltoid insertion—lies *above* the nutrient foramen and not below it, as would be required on the embolic view.

(*b*) If bone deposits are disseminated by the blood stream it seems reasonable to argue that the cases in which they occur should shew pulmonary metastases with especial frequency.

As a matter of fact deposits in the lungs were only present in 24 per cent. of the 37 cases shewing extensive bone deposits or spontaneous fractures, while pulmonary metastases are recorded in 26 per cent. of the entire series of 329 cases. On

the other hand, deposits in the liver were present in 46 per cent. of the cases shewing bone cancer, while they occur in only 42 per cent. of all cases.

These figures on the whole offer no support to the current theory that bone metastases are produced by way of the blood. For there is no marked difference in the incidence of visceral metastases between the cases which shew bone deposits and the cases in which they are absent.

It is true that M. B. Schmidt* has recently shewn how occasionally small cancerous emboli lodged in the lungs may grow along the capillaries and small pulmonary veins, and may thus give rise to systemic embolism without producing any macroscopic changes in the lung. But these cases must be somewhat exceptional, and cannot entirely invalidate the preceding argument.

(*c*) But the weightiest argument against blood infection as a cause of bone deposits lies in the entire escape from metastases of the tibia and fibula, the radius and ulna, the bones of the hand and foot. These bones are just as liable to embolism as the femur or the humerus—probably more so, on account of their greater nearness to the periphery of the circulation—and yet metastases in them are of the rarest occurrence.

B. *Are bone metastases a secondary result of centrifugal growth along the deep fascial lymphatic plexus?*

The fact that the bones nearest the primary growth are more frequently, and those farthest from it most rarely, the seat of metastases, might seem at first sight to suggest that there is actual continuity of growth along the skeleton from the primary cancer outwards to the distal extremities. But the breaking up of the skeleton into distinct segments separated by joints makes such a hypothesis untenable. And evidence has already been adduced that the centrifugal spread of breast cancer takes place primarily along the deep fascia. As in the case of subcutaneous nodules, the irregular incidence of bone metastases within a definite area marks them as casual secondary results of the fascial infection. Such a view accounts satisfactorily for the progressively increasing immunity of the more distal bones.

* M. B. Schmidt, "Die Verbreitungswege der Karzinome," p. 53 (Jena, 1903).

Since there is no suggestion that the growth spreads primarily along the skeleton by continuity, it is not to be expected necessarily that growth will always begin at the proximal end of each bone and extend along it to the distal end. Indeed, a moment's reflection convinces one that such an event is most unlikely. For if the humerus and femur are invaded from the lymphatic plexus of the deep fascia, *the first attack should be directed on that point at which the bone lies nearest to the deep fascial lymphatics, and therefore on that point at which the bone comes nearest to the cutaneous surface.* Moreover, in the case where a bone is provided with two or more subcutaneous areas, the seat of first attack, according to the view of centrifugal spread, must be that area which is nearest to the trunk. Thus, on the hypothesis we are discussing, the point of invasion of the femur should be, and in point of fact is, the base of the great trochanter and the adjoining part of the linea aspera. The point of invasion of the humerus should be, and actually is, relatively much lower down, at the Deltoid insertion, since the whole of the upper half of the humerus is well clothed by muscles.

Centrifugal extension, therefore, explains the peculiar seats of election of spontaneous fractures of the humerus and femur in a far more satisfactory manner than embolic infection by way of the blood stream.

There is no need to insist further on the explanation it affords of the immunity of the bones distal to the knee and to the elbow. These bones escape simply because the patient dies almost invariably before growth has spread along the deep fascia far enough to reach them.

Coincidence of the Areas liable to Bone Metastases and to Subcutaneous Nodules.

It will not have escaped notice that *bone deposits only occur in bones which lie partially or wholly within the area liable to subcutaneous nodules.*

Among the seventy-three cases of bone deposit or fracture with which this Paper deals, there are two which offer apparent exceptions to this rule.

(1) In Case III., Table III., there were bone deposits in the left humerus, both femora, the right tibia, and the right patella. The right femur was infiltrated in its whole length. *The right knee-joint was ankylosed*, and there was growth at the back of the patella and in the head of the tibia. There was osteo-arthritis of the left knee-joint.

Owing to the osteo-arthritic ankylosis of the knee-joint the tibia and patella were practically continuous with the femur. So far, therefore, from weakening the evidence for centrifugal spread, this case strengthens it.

(2) In Case IV., Table III., the body presented a deformed appearance, the limbs being much distorted and the spine curved. Both humeri were fractured, the left at the mid-shaft and the right at the lower third. The left clavicle and the left femur were fractured, the latter two inches below the great trochanter. All these fractures had united. The third, fourth, and fifth right metacarpals shewed un-united fracture.

This case forms the only real exception to the rule just stated. It is quite conceivable that in rare cases the patient may survive until centrifugal extension has involved every bone in the body, and this case seems to be an approximation to that condition. It is worthy of note that the patient had considerable powers of resistance and repair, as is shewn by the fact that all the proximate fractures had united. On the other hand the distal fractures, though they occurred in bones in which quick repair is usual, were un-united. On the centrifugal hypothesis this non-union of the metacarpal fractures is easily understood, because the growth could only have reached them at a very late stage of the disease. A close perusal of these cases shews that with this single exception (which is not in itself conclusive) the rule enunciated at the beginning of this paragraph is an absolute one. *Metastases do not occur in bones lying entirely outside the area liable to subcutaneous nodules.* Nevertheless it is not quite true that the areas of subcutaneous nodules and of bone metastases absolutely coincide. Whenever a long bone such as the femur is invaded, the growth spreads rapidly along the medullary canal, and soon involves the whole length of the bone. Hence the only areas free from bone invasion are the parts distal to the knee and to the elbow.

The fact that bone metastases do not occur in bones lying outside the area liable to subcutaneous nodules may be emphasized by comparing an extreme instance of each condition:—

Bone Deposits.

Plaster-cast No. 673, St. Thomas's Hospital Museum.—The body of a woman who died from scirrhus of the right breast. The skeleton has undergone great distortion. The sternum and ribs have sunk until the former almost appears to touch the vertebral column, the whole thorax being flattened out transversely. The pelvis exhibits a precisely similar modification. The right humerus and both femora have undergone fracture. Right humerus fractured near Deltoid insertion, right femur just below the middle, left femur higher up. (See Fig. 5, which is a photograph taken from the cast of this case.)

Subcutaneous Nodules.

Dr. Rolleston's Case, Clinical Society's Transactions, 1901, p. 206.—Cancer of left breast. Subcutaneous nodules distributed irregularly over the whole surface of the body except the distal portions of the limbs. The nodules extend down the left arm below its mid-point, down the right arm to the level of the anterior axillary fold. They have extended to both groins, reaching on the right side a hand's breadth below Poupart's ligament. Fracture of the left femur occurred in a late stage of the case. (See Fig. 1, p. 31.)

The diagrams on p. 47 indicate the areas liable to subcutaneous nodules and to bone metastases respectively.

The existence of a relationship between bone deposits and subcutaneous nodules is further brought out by their frequent association in the same case. Subcutaneous nodules were present in 22 per cent. of the whole series of 329 cases, while they occurred in 27 per cent. of the 73 cases with bone deposits, and in no fewer than 40 per cent. of the 20 cases which shewed extensive bone deposits, as indicated by metastases or fractures in the femur or the cranial bones.

In the preceding pages a considerable weight of evidence has been brought forward to shew that both subcutaneous nodules and bone metastases result from far-reaching centri-

fugal growth of cancer in the parietes, but the question in which layer of the parietes cancer primarily spreads still remains to be settled.

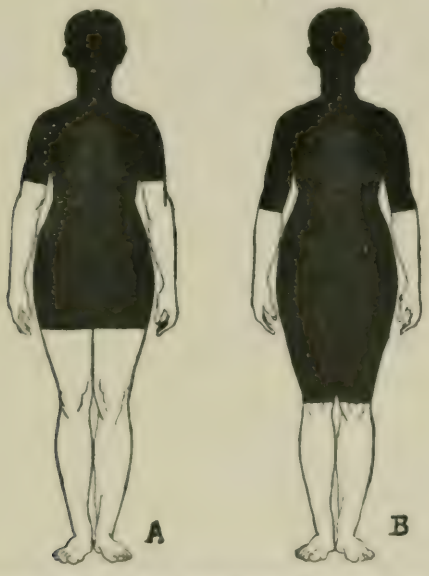

FIG. 4.—Diagrams shewing the Maximal Distribution Areas of Subcutaneous Nodules and of Metastases in Bone in Cases of Mammary Carcinoma. The black area in A is the area liable to Subcutaneous Nodules, that in B is the area within which Bone Metastases occur.

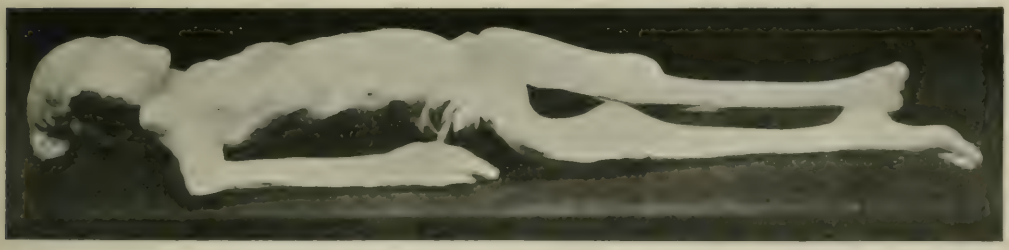

FIG. 5.—Photograph of Plaster Model, No. 673, St. Thomas's Hospital Museum, by kind permission of Mr. Shattock.—The body of a woman who died of Scirrhus of the Right Breast. The figure is inserted to illustrate the immunity of the bones distal to the knee and elbow, even in an advanced stage of Secondary Bone Cancer.

Is it possible from clinical evidence definitely to decide whether centrifugal growth takes place along the skin and subcutaneous tissue or along the deep fascia?

The problem is one of immense importance for the future operative treatment of cancer of the breast. Removal of the skin has reached already its furthest possible limits, and it is therefore not surprising if surgeons who hold that cancer spreads along the skin believe that no great improvement upon present results is likely to be attained. Thus Halsted, who invariably removes so much skin that he is unable to sew up the wound, says: "When operating for cancer of the breast we cannot be responsible for undiscoverable metastases in the skin. For the principal growth, the axilla, the pectoral muscles, and the supra-clavicular region—in other words, for the scar in its fullest sense—we should hold ourselves responsible, but for the eradication of the so-called lenticular and apparently discrete metastases of the skin we have no guide. One might literally flay the patient's chest and side, only to find, weeks or months later, one or more cancer nodules in the skin of the neck, or the back, or abdomen."

Cheyne,* too, says: "I think that we may now form a fairly final judgment with regard to the treatment of cancer of the breast by operation."

But if the accepted theory of the spread of cancer is wrong—if breast cancer instead of spreading along the skin spreads along the deep fascia, and only here and there blossoms outwards into skin nodules—the results of operation are certainly capable of improvement, for it is possible to remove the deep fascia over a wider area than has ever yet been practised.

In my opinion a most important indication in this direction is afforded by a comparison of the operative methods and results of Cheyne and Halsted, who may be regarded as among the protagonists of breast surgery on this and the other side of the Atlantic.

Both operators practise a wide removal of skin; but whereas Cheyne generally succeeds in sewing up the wound, Halsted has usually to resort to skin grafting. It may be assumed therefore that the American surgeon removes rather more skin than does his English colleague.

On the other hand, Cheyne lays special stress on the undermining of the skin all round the incision. He says: ". . . . the skin incisions when made should not go straight down to

* "Lancet," March 12th, 1904.

the muscle. After the skin incisions have been mapped out, the skin and just sufficient fat to enable it to retain its vitality should be dissected up, and the muscular fibres should not be exposed till just below the clavicle above, beyond the middle line in front, over the region of the abdominal muscles below, and over the edge of the latissimus behind."

Halsted, on the contrary, nowhere refers to the undermining of the skin so as to secure removal of an area of deep fascia wider than that of the skin removed. His skin incisions "are carried at once and everywhere through the fat." Then in removing the breast: "the whole mass, skin, breast, areolar tissue and fat, *circumscribed by the original skin incision* (italics not in the original), is raised up with some force, to put the submuscular fascia on the stretch as it is stripped from the thorax close to the ribs and pectoralis minor."

The differences in other respects between the two operators are unimportant for my present purpose. What I would lay stress upon is that while Halsted removes more skin than Cheyne, Cheyne carries out a far freer ablation of the deep fascia than Halsted.

A study of the results of the two operators with regard to local recurrence should therefore give valuable indications. If cancer spreads centrifugally along the skin, Cheyne's wide removal of the deep fascia is evidently a vain precaution, and Halsted's extensive removal of skin is correct. If, on the contrary, cancer spreads along the deep fascia and only secondarily invades the skin, Halsted's free removal of skin will be invalidated by his failure to remove the more widely infected deep fascia around his wound.

The records of local recurrence in the two sets of cases will be found summarized in the table on the following page.

This table shews that the practice of removing a very wide area of deep fascia and a less wide area of skin gives better results than the removal of less fascia and more skin.

Taking skin recurrences only, Halsted gets 16 per cent. and Cheyne 6·5 per cent. If the latter's three cases of local recurrence of unknown position be all counted as skin recurrences his percentage is raised to 11 per cent., but even then the difference is still one in favour of the operation with wide removal of deep fascia.

TABLE II.

SHEWING THE COMPARATIVE RESULTS OF VERY WIDE REMOVAL (*a*) OF SKIN, (*b*) OF DEEP FASCIA, IN BREAST CANCER.

Operator.	No. of cases.	Practice as regards removing		Percentage of successes.	Percentage of external recurrences.	Situation of External recurrences.		
		Skin.	Deep Fascia.			Local recurrence, position unknown.	Pectoral muscles or ribs.	**Surrounding Skin.**
Halsted	50	very wide removal.	removal coterminous with that of skin except towards axilla, where it is greater.	41 per cent.	21 per cent.	..	3 cases =6 per cent.	**8 cases =16 per cent.**
Watson Cheyne	61, 1st series	wide removal.	very wide removal.	upwards of 50 per cent.	18 per cent.	3 cases =4·9 per cent.	4 cases =6·5 per cent.	**4 cases =6·5 per cent.**

We arrive then at the anomalous result that *the operator who removes the smaller area of skin yet has a lower percentage of skin-recurrences*, a result which goes far to prove that breast-cancer does not spread primarily in the skin, but simply here and there extends to it from the deep fascia.

In the next place these conclusions are strengthened by a study of the *site* of the skin recurrences. Cheyne mentions the site of recurrence in two cases. In one of these a skin nodule developed near the angle of the scapula, in the other at the edge of the latissimus dorsi. In four of Halsted's cases the recurrence was at the outer, or lower and outer, side of the scar, and in one over the opposite breast.

Thus, although Cheyne removes less skin than Halsted, yet his skin recurrences are situated further away from the site of primary growth.

And finally, a glance at Halsted's sketch of the parts removed by his operation shews that his removal of the deep fascia is at its minimum along the inner, and along the lower and outer sides of the breast, situations at which skin nodules developed in at least five of his eight cases.

Conclusions.

(1) The study of secondary growths in the skin and subcutaneous fat, and in the bones, affords clear evidence of a slowly progressive, centrifugal, quasi-serpiginous spread of breast-cancer in the parietes in continuity with the primary growth, and independent of the flow of lymph or blood.

(2) The scattered and isolated character of the deposits in the skin and bones indicates that it is not along these layers that the growth primarily spreads.

(3) A study of the results of operation where (*a*) much skin and fascia, (*b*) less skin and more fascia are removed, strongly suggests that parietal extension does not take place primarily along the skin, but along the deep fascia, with secondary lateral off-shoots (*a*) towards the surface, as subcutaneous nodules, (*b*) towards the deeper tissues, as bone (or muscle) deposits.

III.—MODIFICATIONS IN OPERATIVE PROCEDURE SUGGESTED BY THE PRECEDING CONSIDERATIONS.

(i) Removal of Skin.

Wide removal of the skin is necessary, owing to the vertical extension to it, after a time, of the growth which is spreading in the deep fascia; but removal of such an extent as interferes with subsequent approximation of the edges of the wound seems to be unnecessary, save in exceptional cases.

If after the primary operation skin nodules appear in the neighbourhood, *their significance depends on whether they lie within the area from beneath which the deep fascia has been excised or outside it.*

In the former case they are to be regarded merely as local deposits—"efflorescences"—whose roots have been already removed, though at the time of the operation they themselves were too small to be detected. Such nodules can, therefore, be excised with every prospect that recurrence in the neighbouring skin will not take place.

On the other hand, subcutaneous nodules appearing in an area where the deep fascia is still intact indicate wide extension of the growth in the latter layer. If they extend far from the original primary growth the case must probably be regarded as hopeless, owing to the large area of fascia involved.

(ii) Removal of the Deep Fascia.

It has been explained that the invasion of the fascial lymphatic plexus is in no way limited by the boundaries of the pectoral fascia. *The aim should, therefore, be to remove as widely as is practicable a circular area of deep fascia with its centre at the primary growth,* remembering, however, that growth extends in the fascia rather more readily in a vertical than a horizontal direction.

The use of the expression "removal of the pectoral fascia" instead of "removal of as wide an area as possible of the deep fascia," and the exclusive attention paid to the axillary glands as the channels of dissemination have led to neglect in the excision of the deep fascia over the lower part of the thorax and the upper part of the abdomen. It seems to be in this direction that the scope of the operation requires extension, rather than in the direction of opening up the posterior triangle.

The following measurements shew the distance from the nipple to various points on the thorax in two patients with non-pendulous mammæ :—

	Patient No. 1.	Patient No. 2.	Average.
Nipple to tip of ensiform cartilage... ...	4 in.	5 in.	4½ in.
Nipple to nearest point of clavicle	5 in.	6¼ in.	5¾ in.
Nipple to nearest point of middle line ...	3½ in.	4½ in.	4 in.
Nipple to nearest point of edge of latissimus dorsi	—	5 in.	5 in.

The distance from the nipple to the clavicle may be taken as the radius of the circle of deep fascia round the growth, which can, in practice, be removed without difficulty by undermining the skin flaps sufficiently and prolonging the incision somewhat in a downward direction.

If the growth starts under the nipple the deep fascia should accordingly be removed—

above ... ... up to the clavicle,
internally .. 1 to 2 inches beyond the middle line,
externally .. just beyond the anterior edge of the latissimus dorsi,
below ... ... *to a horizontal line running at least 2 inches below the tip of the ensiform cartilage.*

If the growth is in the lower and inner part of the breast the circle of infected deep fascia will encroach still more on the surface of the abdomen, and over the opposite side of the breast, and removal of the deep fascia in these directions must be carried out yet more widely.

It has often been considered sufficient, wherever the growth is situated, to remove the whole breast, its lymphatics (and therefore the pectoral fascia and part of the great pectoral muscle), the lymphatic tract running to the axilla, and the axillary contents. This aim, however imperfect, gives good results when the growth is central in the breast. But when the growth is peripheral the circle of infected fascia is almost certain, by the present mode of operating, to be intersected and partially left behind in one or other direction.

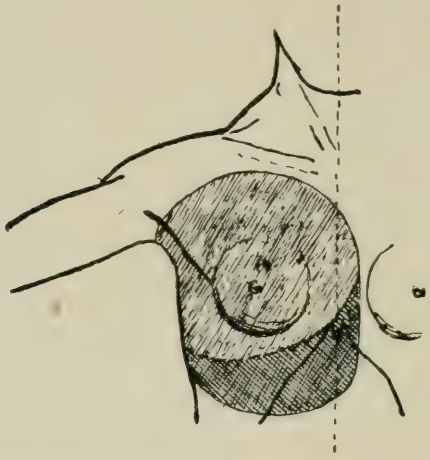

FIG. 6.—The lightly-shaded area represents the extent of deep fascia removed in the operation of excision of the breast, as at present usually performed.

The darkly-shaded area represents the additional extent of deep fascia which should, in future, be removed to ensure that the circle of invaded fascia shall be completely circumscribed and not intersected below.

The line surrounding the whole shaded area represents the extent to which the skin-flaps should be undermined for that purpose.

It is probable that the want of coincidence between the area of the present operation and the circle of infected fascia in these eccentric growths largely accounts for the bad prognosis associated with them.

Even when the growth is central the present operation removes far too exiguous a portion of deep fascia in a downward direction. Cheyne, who carries out ablation of the fascia as widely as any one, recommends that it should be removed below,

"over the origin of the abdominal muscles." The expression is somewhat vague, and both the rectus and the external oblique muscles are attached well above the costal margin. It is, therefore, unlikely that Cheyne's removal of fascia extends further than the costal margin, if as far; and under these circumstances it is almost certain that in some cases, while circumscribing the infected area of deep fascia above, externally and internally, his operation will intersect it below and leave a part of the infected area. Fig. 3, p. 37, which illustrates an advanced stage of infection of the fascial plexus lying on the rectus sheath, shews that this is no merely theoretical danger.

In order to obtain access to the upper part of the abdominal wall for the purpose of removing its deep fascia, the lower angle of the incision should be prolonged downwards for two or three inches over the linea alba, and the flaps undermined to a corresponding extent. Great care should be taken to remove every particle of the origin of the pectoralis major from the rectus sheath. The surface of the latter on both sides of the middle line should be most carefully cleaned—as should also the digitations of the muscular part of the external oblique—down to a horizontal line running two or even three inches below the tip of the ensiform cartilage.

TABLE III.—Secondary Deposits (or Fractures) in the Femur in 329 Cases of Mammary Carcinoma.
(Middlesex Hospital, 1872—1901.)

Case.	P.M. Number.	Site of primary growth.	Femur affected and Site.		Other bones affected.	Details.
			Right.	Left.		
I.	201, 1883	L.	Fracture 1 inch below great trochanter.	Fracture rather lower than on right side.	Right humerus fractured during the autopsy.	No cancer in connection with any of the fractured bones. Fracture of right femur repaired by a large mass of callus; not much reparative material round fractured left femur.
II.	16, 1885	R.	No details of site.	.. ..	Right humerus infiltrated and fractured.	The right femur shewed extensive infiltration of the medullary cavity, with perforation of the bone at one spot.
III.	14, 1886	L.	Infiltrated throughout, but most in its upper part; three fractures.	One inch below lesser trochanter; fracture at this point.	Left humerus, right tibia and patella (ankylosis of right knee-joint).	Right femur fractured in three places: neck, upper third, junction of middle and lower thirds. Bone distorted and in great part replaced by growth. Its outline still traceable in its lower third. Right knee ankylosed; chronic osteo-arthritis of left knee.
IV.	57, 1888	?	.. ..	Fracture 2 inches below great trochanter.	Both humeri, clavicle and three metacarpals fractured, ribs brittle.	The presence of cancer in the bones is not stated.
V.	280, 1891	L.	.. ..	Fracture just below trochanter.	Both humeri, cranial bones, spine, sternum, ribs.	Left femur fractured. Growth is stated to be present in some of the bones, but its presence in the left femur is only implied.

VI.	11, 1873	R.	Fractured at upper end.	.. ..	None.	Right femur fractured; false joint surrounding growth as large as fœtal head.
VII.	101, 1876	R.	.. ..	Just below trochanter.	None.	A large mass of osteoid cancer round the left femur, just below trochanter.
VIII.	160, 1879	R.	.. ..	Fractured in its upper part.	None.	Impacted fracture; no statement as to growth at site of fracture.
IX.	22, 1882	L.	.. ..	5½ inches from tip of great trochanter.	None.	Spontaneous un-united fracture; no statement as to presence of growth.
X.	212, 1885	Both breasts.	Fractured at junction of shaft with great trochanter.	?	Four ribs.	Fracture of right femur at site of deposit, where there was a mass of cancer the size of a man's fist, with some calcareous deposit in it. The medulla here invaded, the cortex of the femur destroyed. Head of the bone soft and wasted, but not cancerous.
XI.	183, 1892	L.	Fractured 4 inches below head, also through neck.	Six inches below neck.	Sternum, clavicle.	New-growth found over the right great trochanter, and again about 3½ inches below this. Three inches below the lower fracture the shaft of the bone shews no new growth. No deposit of new-growth was seen about the left femur, but on removal it was found plugged with growth, reaching up ½ inch above the fracture, above which the medulla is natural.

TABLE III.—*continued.*

Case.	P.M. Number.	Site of primary growth.	Femur affected and Site.		Other bones affected.	Details.
			Right.	Left.		
XII.	135, 1893	R.	Fractured just below great trochanter.	.. ..	Sternum.	On dissecting down over the shaft of the right femur a cavity is exposed containing 10 to 20 ounces of cholocate-like fluid, within which the two rough ends of the fractured bone can be felt. The new-growth was chiefly confined to the upper fragment, involving the great trochanter, which was largely destroyed, and the shaft just below it.
XIII.	163, 1898	R.	Upper two-thirds infiltrated.	.. ..	Sternum, four ribs, frontal and parietal bones.	Upper two-thirds of shaft of right femur infiltrated; two old un-united fractures present, one ? 2 inches below the neck, the other 2¼ inches lower down.
XIV.	71, 1900	R.	Fracture near upper end.	Fracture near upper end.	Frontal bone, 8th and 9th thoracic vertebræ.	Thighs much shortened and deformed by swellings at the upper end. In left femur growth invades both medullary cavity and periosteum. In the right femur the growth is less extensive, and scarcely invades the periosteum, but only the medulla of the bone. Both femora are fractured.

TABLE IV.—Secondary Deposits (or Fractures) in the Humerus in 329 Cases of Mammary Carcinoma. (Middlesex Hospital, 1872—1901.)

Case.	P.M. Number.	Site of primary growth.	Humerus affected and Site.		Other bones affected.	Details.
			Right.	Left.		
I.	201, 1883	L.	Fracture just above elbow joint.	.. ..	Both femora.	"No cancer in connection with any of the fractured bones."
II.	16, 1885	R.	Fracture, upper two-thirds infiltrated.	.. ..	Right femur.	Right humerus fractured.
III.	14, 1886	L.	.. ..	Infiltrated throughout, but most above.	Right tibia and patella, both femora.	The left humerus, infiltrated throughout with cancer, measured on section nearly 3 inches about the level of the surgical neck, gradually tapering off to the lower end, where it was very thin, and the bone had been fractured in two places.
IV.	57, 1888	L.	Fracture lower third.	Fracture mid-shaft.	Clavicle, 3rd, 4th and 5th R. metacarpals, and left femur fractured.	No definite statement as to growth in the bones; ribs very brittle.
V.	280, 1891	L.	Fracture at Deltoid insertion, whole length infiltrated.	Fracture at Deltoid insertion.	Left femur fractured, growth on ribs, cranial bones, spine, sternum.	The right humerus in the whole of its medullary portion is occupied by pale new growth. Condition of left one not stated.

TABLE IV.—*continued.*

Case.	P.M. Number.	Site of primary growth.	Humerus affected and Site.		Other bones affected.	Details.
			Right.	Left.		
VI.	116, 1874	Both ?	Site not stated.	.. ..	Spine, right parietal and frontal bones, and basis cranii.	Right humerus broke at autopsy. Its medullary canal infiltrated by cancer.
VII.	87, 1880	L.	Fracture lower third.	.. ..	Sternum.	Right arm œdematous. Swelling most marked in its lower third, where from its mobility the bone was evidently broken. No definite statement as to presence of growth.
VIII.	162, 1899	L.	Fracture just below junction of middle and lower thirds.	.. ..	.. ..	A secondary deposit in the shaft of the right humerus.
IX.	58, 1900	R.	.. ..	(?)Fracture mid-point. (See Details.)	Parietal bones.	There is well-marked bending of the left humerus forwards, with considerable thickening of the bone near its mid-point.
X.	176, 1873	..	.. ..	.. ..	.. ..	Humerus involved by an extension of growth from the axilla. Details could not be found.

THE OTTO SCHMIDT TREATMENT FOR CANCER.

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A Paper was read by Dr. Jossé Johnson before the Abernethian Society of St. Bartholomew's Hospital on 5 November 1903, in which it was alleged that Dr. Otto Schmidt had discovered a "cure" for cancer. Although it was at the time considered strange that a Students' Society should be chosen rather than one of the great Medical Societies of London for a pronouncement of this importance, nevertheless one of the duties of our Hospital is to enquire into all such discoveries and, if advisable, to subject them to trial in the wards. The object of the present Paper is to give the results of our experience with Dr. Schmidt's material, and, incidentally, to indicate the lines upon which examination of a new method of treatment for cancer is carried out in the Middlesex Hospital.

The foundation of Dr. Schmidt's treatment lay in the fact that he had, so it was asserted, discovered the specific cause of cancer. Such a discovery was certainly within the range of possibility, because for many years the various theories purporting to explain the causation of cancer have essentially been reduced to two: firstly, that the structural changes in the cells of the affected part are due to the presence of a parasite, and, secondly, that these changes result from an error of development, which may be congenital or acquired.

Having laid claim to the isolation and cultivation of a cancer parasite, Dr. Schmidt further contended that from this parasite he had been able to manufacture a remedy, which he procured in two different ways.

In the one, the cultivations of the parasites were sterilized and a pure "Killed culture" obtained. This was injected in small but increasing doses. It was considered to be the more satisfactory material of the two, and was the only one used in the investigation at the Middlesex Hospital. In the other a serum was obtained from an animal which had been previously inoculated with increasing doses of "cancer parasites." This serum was also injected subcutaneously.

The first information which the English medical world had of this new treatment were the bare facts contained in Dr. Johnson's communication that these "parasites" had been isolated, that methods of treatment had been devised, and that "twenty-nine cases had been dealt with successfully," a typical case being set forth as follows :—

"It was that of a woman who had undergone no fewer than six operations for the removal of cancer of the breast. She also had a malignant growth on the forehead, which it was considered quite hopeless to try and remove. As a result of Dr. Schmidt's treatment by injections there was a great gain in the patient's general health, and the growth on the forehead shrank to a mere scar. As far as could be told, the woman, without the treatment, in the natural course of the disease would have died shortly, but she was progressing well when last seen."*

Arguing from a scientific standpoint, we should have expected Dr. Schmidt to have subjected the whole process of his "discovery" to scientific criticism before prematurely announcing to the world that he had discovered a "cancer cure."

Judging from other "discoveries" on the same lines, we are bound to demand absolute proof that the subjects treated are really suffering from cancer by the exhibition of sections of the growth prepared for the microscope: we must be shewn cultivations and microscope preparations of the parasite; we must be told the exact and detailed methods by which the remedy is obtained, and we must see one or more of the patients so treated before, during, and after the process of cure. Not in any one of these particulars did Dr. Schmidt satisfy the Medical Profession.

Besides producing a cure, Dr. Schmidt is understood to have stated that his therapeutic media were suitable for diagnostic

* The patient died early in 1904; the post-mortem and microscopic examination gave complete evidence of carcinoma.

purposes, since patients with undiscovered cancer reacted in a peculiar manner, whereas non-cancerous persons failed to react entirely. Since the specific temperature reaction was said to occur about six hours after injection, a two-hourly chart was kept in the case of all the Middlesex patients for the ten hours immediately succeeding each injection.

We shall shew later, when describing cases of *undoubted* cancer so treated, that no reaction whatever took place.

Nine patients were, with their consent, subjected to the treatment, but in one case treatment was discontinued. The cases were selected by Dr. Jossé Johnson and the Hospital Medical Officers, and Dr. Schmidt, when visiting the Hospital on 28 November, expressed himself satisfied with them for test purposes. After selection, and before treatment was commenced, the affected parts were photographed. Most careful notes were taken of the distance from the camera, length of exposure, etc., in order to possess data for another exactly comparable set of photographs at a later date. In point of fact it never became necessary to take this second series of photographs.

Each case was re-examined before commencing treatment, and the actual condition compared with the description in the notes, and when agreement was arrived at the description was initialled by Dr. Jossé Johnson and by the Director of the Cancer Laboratories. In making the subsequent notes strict impartiality was observed, and notes were initialled in case of divergence of opinion. It is only fair to Dr. Jossé Johnson to state that, although he commenced the course of treatment prejudiced in its favour, he ended by becoming thoroughly convinced of its inefficiency.

Case No. 1.—Annie R., aged 59, carcinoma of right breast of one year's duration. No operation had ever been performed and the growth began to ulcerate in September 1903. She was admitted into the Cancer Wards on 6 November 1903. The condition then was as follows:—

A fairly well-nourished woman. The growth occupied the whole of the right breast and was rounded in general outline. The skin was adherent over the most part and was ulcerated at the centre of growth. The nipple had ulcerated away.

The tumour measured 3 inches both in its vertical and transverse diameters, and was firmly fixed to the chest-wall. There was an area of infiltration extending upwards and outwards towards the right axilla, and this was hard and puckered, forming a deep groove in the skin. The right axilla was occupied by a mass of hard, adherent glands. The left breast was free from disease. The liver was not enlarged, nor was there any evidence of secondary deposits in bone.

The treatment commenced on 26 November 1903, when one-tenth of a milligramme of Dr. Schmidt's "Killed culture" was injected beneath the skin of the left supra-clavicular fossa.

27 November.—No local pain during the night, no ulceration in breast. Half a milligramme injected into thigh.

28 November.—One milligramme was injected in left thigh. Dr. Johnson noticed a defined edge on the inner and under sides of the ulcerated area which, he said, was not there yesterday.

30 November.—No defined edge visible this morning; ulcerated surface covered by a sloughy mass of the exudation. Five milligrammes injected into left thigh in concentrated solution. Patient was shivering this morning; temperature 98°. External temperature (air) cold.

1 December.—On the inner side of the left breast is a small mass about the size of a Spanish nut, quadrilateral in shape, in the substance of the gland, freely movable, and slightly tender. No enlarged glands on that side. Patient is not shivering this morning; temp. 98°. The surface of the exudation on ulcer is slightly more translucent. Ten milligrammes injected into thigh.

Injections were continued daily in gradually increasing doses until 2 centigrammes were given on 8 December. There was no change to note in the condition of the growth.

9 December.—At 1.30 in the afternoon patient was seized with a syncopal attack. This was the third similar attack the patient has had since admission, but the first since the particular treatment was commenced. There was no reason to associate its occurrence with the injections.

10 December.—One and a half centigrammes injected to-day. Very poor pulse. No other change to note. This was the last injection given. Ten injections were given in all.

On 14 January it could be seen that the patient was rapidly emaciating and that the disease was pursuing its course unchecked. From this time the patient passed into a state of drowsiness, gradually deepening into coma, and died on 19 January 1904.

Post-mortem and Microscopical Report.—The right breast was entirely occupied by growth and fixed to the chest-wall. There was a nodule in the left breast. Secondary deposits had taken place in both lungs, in the liver, uterus, and kidneys.

Microscopically the growth was a spheroidal-celled carcinoma, and the various secondary deposits were of similar structure. The appearances were in no way different from those met with in similar cases that had not been treated with Dr. Schmidt's material, either as concerns the primary growth or as concerns the metastases.

Case No. 2.—Caroline A., aged 56. There was no family history of cancer. The patient first noticed a small lump in the right side of the neck just above the clavicle.

Nine months before admission the swelling was at first quite painless, but had been gradually growing larger and painful. No operation was performed at any time. There was no difficulty in breathing or in swallowing.

She was admitted into the Cancer Wards on 21 September 1903, when she stated that she had lost about a stone in weight during the past nine months.

The condition on admission was as follows:—

The patient appeared to be slim generally, but not emaciated. There was a hard tumour in the right posterior triangle of the neck quite fixed to the underlying tissues. The surface was nodular; no fluctuation was felt at any part. The general outline of the tumour was globular, with a diameter of 1½ inches. The nerves of the cervical and bronchial plexuses were involved by the growth, and pain was experienced in the areas of their distribution. There was no evidence of growth in the mouth, throat, larynx, scalp, breast, or mediastinum. A few scattered enlarged glands were present behind the main swelling. The liver was not enlarged, and no enlarged glands were felt in the axilla or on the opposite side of neck.

The patient was being treated with the X-rays from June 1903, and this was continued until the commencement of the Schmidt treatment on 26 November.

On 29 October it was noted that patient had for several days been spitting up thick blood-stained sputum.

The growth was very painful. The general range of temperature was between subnormal and 101·4°.

26 November.—One-tenth of a milligramme of "Killed culture" was injected into the subcutaneous tissues of the left supra-clavicular fossa, and it was noted that the skin was loose over the tumour, and that there was no redness.

Injections were given in gradually increasing doses, reaching 10 milligrammes on 1 December.

There was no change to note in the growth; no special rise in temperature. Sputum less blood-stained.

3 December.—It was specially noted on this occasion that there was a tongue-like outgrowth, tender on pressure, extending backwards over the supra-spinatus muscle. The main mass was apparently slightly movable, and a fresh enlarged gland could be felt above it.

8 December.—Injections were gradually increased to 2 centigrammes given this morning. Slight swelling and tenderness over seat of past injections. No change in growth. For the past two days there had been marked alterations in the voice, the patient only speaking in a whisper. Laryngoscopic examination shewed the larynx to be very red; the cords were swollen and red, and moved slightly during respiration.

10 December.—No injection to-day as patient did not feel so well. Much tenderness over swelling, and pain in neck. The main growth was slightly larger, but the tongue-shaped portion behind was smaller. No more injections were given. In all ten injections were given during the treatment.

16 January 1904.—The skin had ulcerated over the growth, leading to sanguineous discharge and a marked diminution of the bulk of the growth. Expectoration deeply blood-stained and foul; emaciation proceeding rapidly.

28 January.—Breathing became very laboured and death took place.

Post-mortem and Microscopical Report.—The tongue, larynx, pharynx, and œsophagus were free from new growth. The

lymphatic glands on both sides of the neck, together with the mediastinal glands, were the seats of new growth. Lymphatic glands in other situations were free. The right upper lobe of lung was involved in the growth by a continuity from that of the bronchial and mediastinal glands.

The microscope revealed a spheroidal-celled carcinoma; abundance of fibrous tissue was present, and scattered throughout were masses of epithelial cells lying in alveoli. The cells were polyhedral in shape.

Case No. 3.—Edwin J., aged 60, carcinoma of rectum. No family history of cancer. Syphilis thirty-five years ago.

The patient was troubled with piles in March 1903. About this time he noticed a "stiff feeling" in rectum, and passed a good deal of mucus mixed with blood. He saw a surgeon who found a "growth" on the posterior of the rectum, low down, and excised it. He was not able to walk much after the operation, although his general health improved.

He was admitted into this Hospital on 23 November 1903, the local condition being as follows: A hard indurated mass was present on the posterior and left walls of rectum, about 2½ inches from the anus. The mass was fixed to the sacrum. The surface of the growth was shreddy to papillomatous. The fixity of the growth negatived any operative interference.

The Schmidt treatment commenced on 30 November 1903, when four-tenths of a milligramme was injected into the right forearm. It was continued until 21 January 1904, in gradually increasing doses, which ultimately reached a maximum of 2 centigrammes.

During this interval there was no change of any kind which could be set down to the effects of the treatment. Pain varied from time to time, and there was no reaction shewn either by rises of temperature or local condition of growth.

Patient was discharged at his own request on 27 January 1904. A local examination shewed that the condition of the growth was unchanged, while at the same time there had been no appreciable extension of the growth, the polypoid masses remaining the same.

Treatment was continued outside the Hospital by Dr. Jossé Johnson, and from first to last 131 (?) injections were given.

Thirty-five injections were given while the patient was in the Hospital. The patient was re-admitted on 10 March for great pain and partial obstruction owing to the increased size of the growth. Lumbar colotomy was performed on 15 March, but the patient developed pneumonia and died on 21 March 1904.

Post-mortem and Microscopical Report.— The rectum was the seat of a large crateriform ulcer, the edges of which were raised and indurated. The ulcer had a diameter of 2 inches. The liver was enlarged and infiltrated with new growth. Both kidneys appeared to be in a condition of nephritis.

Microscopic examination revealed the growth to be a columnar-celled carcinoma of rectum, which differed in no respect from similar cases in which Schmidt's treatment had not been tried.

Case No. 4.—Frances B., aged 71, a patient of the Cancer Wing since 26 February 1901 with an ulcerating carcinomatous growth of the right breast, measuring on admission 3½ inches transversely and 2 inches vertically. The patient is still living. The growth is fixed to the chest-wall. The patient was treated with the X-rays at various intervals from 9 September 1901 to July 1903, with the result that the growth greatly diminished in size and the ulcerated surface was covered over with a sound layer of epithelium.

The Schmidt treatment commenced on 26 November, and the note made on that day was as follows :—

Bilobed growth, the mass towards the centre about the size of a horse-chestnut, and that towards the axilla about the size of a large cherry. Firm enlarged glands beneath the edge of pectorals, skin over them slightly red. One-tenth milligramme of " Killed culture " injected into the left supra-clavicular fossa.

30 November.—The doses were gradually increased, and on this date 5 milligrammes were given. The growth was slightly more tender. Injection was made into the left thigh owing to pain in previous situation.

1 December.—One centigramme injected into left thigh.

2 December.—A good deal of pain yesterday; increased tenderness in the circumference of the mass, particularly below and internally and in sub-pectoral glands. Tenderness and " bruised feeling " in region of punctures in thigh; skin red.

3 December.—Considerable tenderness in growth. Around the central mass there was a swollen lobulated appearance more manifest than previously. Redness on thigh almost disappeared. Glands beneath pectorals sub-elastic and very tender. There has not been any special rise of temperature.

8 December.—Less tenderness, otherwise no change. Two centigrammes injected into left supra-clavicular fossa.

9 December.—Some swelling and considerable tenderness over the left supra-clavicular fossa (the site of injection). Slight local tenderness. A movable tender gland, the size of a large hemp seed, felt at the inner border of the right sterno-mastoid. 2·5 centigrammes injected into left thigh.

10 December.—On the previous evening temperature rose to 101·4° for the first time. The injection (2·5 centigrammes) was given at 10 a.m., and the rise was noted at 6.15 p.m.

10 December.—The last injection (2 5 centigrammes) was given to-day. In all eleven injections were given. No permanent changes in growth.

May 1904.—The patient is still in Hospital. General condition good. The patient is up and about daily.

The local condition is as follows:—

The lobulated condition of the growth is still characteristic; a fresh nodule has appeared at the lower part. There is no ulceration. The glands under the pectorals are slightly tender. On the whole the growth is slightly larger.

Case No. 5.—Hannah A., aged 56, carcinoma of both breasts.

This patient is still living.

A healthy-looking woman who is deaf and dumb. No history of cancer. She gives a history of having had "something wrong" with her right breast since 1888, but had only noticed a small lump in the left breast for three weeks before admission in 1902.

She was admitted into the Cancer Ward on 7 May 1902, when the condition was as follows:—

The right breast has completely shrivelled away, and is replaced by a warty growth measuring 5 inches transversely and 3½ inches vertically. The whole surface is superficially ulcerated and discharges a thin, slightly-coloured fluid. There are

many enlarged glands in the right axilla and in the right supra-clavicular fossa.

The left breast is the seat of a hard growth surrounding the nipple, from which there is a slight discharge. The breast is freely movable, and there are no enlarged glands in the left axilla.

The skin around the growth of right breast is superficially excoriated for some inches around and presents a bright eczematous appearance. There are no signs of visceral metastases.

For a time the patient was treated with the X-rays and high frequency currents, but these had to be discontinued owing to the intense irritation which they produced.

The Schmidt treatment was commenced on 26 November 1903, and the note made of the local condition on that day was as follows :—

Superficial small granular appearance on a bright red ground, which apparently consists of small nodules of quite superficial growth. The nodules differ much in size, but none are larger than a cherry-stone, and the majority are about the size of a hemp seed. The centre is ulcerated, and the entire mass is $3\frac{1}{2}$ inches in vertical and 5 inches in transverse diameter. The left breast shews similar appearances, but the nipple is still present and not retracted. The measurements are 3 inches transversely and $1\frac{3}{4}$ inches vertically. There are large glands in the right axilla and a small gland in the left. A large hard gland is present above outer end of right clavicle; a small shot-like gland is above inner end. Liver not felt.

26 November.—The treatment began with one-tenth of a milligramme of "Killed culture." The dose was gradually increased to 10 milligrammes, and was generally injected into the left thigh.

1 December.—The ulcerated surfaces are distinctly redder this morning.

2 December.—There is a patch of subcutaneous inflammation at the seat of yesterday's injection, measuring $3\frac{1}{2}$ inches by $3\frac{1}{2}$ inches. One centigramme injected into right thigh. No local change.

9 December.—Dose gradually increased to 3 centigrammes injected into left supra-clavicular region; the injection caused much pain to-day.

There is no change either in the growth or in the glands in the right supra-clavicular fossa.

The last injection was given on 10 December and consisted of 3 centigrammes. In all ten injections were given. At no time was there any appreciable rise of temperature or any other indication that a reaction had taken place.

May 1904.—The patient is still in the Hospital. The disease is progressing, the ulceration is spreading towards the right axilla, the axillary tissues are becoming infiltrated, compressing the lymphatics and leading to œdema of the arm. The general condition is still, however, fairly good.

Case No. 6.—Charlotte B., a stout healthy-looking woman, 73 years of age, quite crippled from poly-articular osteo-arthritis.

Admitted into the Cancer Wards on 2 May 1902.

The patient first noticed dimpling of the skin on the outer side of the left breast at the end of 1900. Skin broke down four months before admission, and an ulcer rapidly formed. The condition on admission was as follows :—

The left breast is the seat of a contracting growth, and forms a deep gutter across the breast, dividing it into two lobes. The growth is firmly fixed to the chest-wall. The ulcerated surface is very red and bleeds easily.

The Schmidt treatment began on 26 November 1903 with one-tenth of a milligramme injected into the right thigh.

The note on this occasion was as follows :—

The local condition was much the same as on admission.

There are no glands to be felt in the axilla, but there is a circular, non-ulcerated superficial plaque 1 inch in diameter just above the left costal margin in mid-axillary line. Considerable tenderness over the more anterior of the two lobes of which the mass consists. No enlargement of liver.

28 November.—One milligramme injected into right thigh.

30 November.—The skin over the internal portion of the mass, and that over the nodule, is slightly redder this morning. The ulcerated surface is a little drier.

The injections were gradually increased, and 3 centigrammes were given on 10 December, this being the last injection. In all eleven injections were given.

At no time was there any rise of temperature, and beyond slight increased pain and redness (which varied from day to day), there was no change in the size of the growth or of the ulcerated area.

The patient is still in the Hospital, and her general condition remains unchanged. A fresh nodule has appeared in the skin on the right side just below the axilla. The ulcerated area of the growth is now somewhat less, owing to the contracting nature of the growth.

Case No. 7.—Emily S., aged 43.

This case was chosen in order to test the alleged specifically diagnostic value of the material, and the doses were raised very rapidly and considerably.

This patient underwent amputation of the left breast for carcinoma in May 1903, and was re-admitted on 21 January 1904 for a swelling in the right breast, which she had noticed for six weeks. She stated that she had been suffering from shortness of breath for two months past, and that sickness had recently been very frequent.

In the upper and outer quadrant of the right breast was a small hard lump about the size of an almond, with an ill-defined edge, movable on the chest-wall. No gland felt on the axilla. At the junction of the second left rib with the sternum was an area of ill-defined dulness of small size. No increased prominence observed at this spot. No glands in left axilla.

Injections began on 29 January, when 1 milligramme was given.

She had six injections altogether, dose increasing up to 2 centigrammes. There was no trace of a local or constitutional change to note, and the patient was discharged.

Case No. 8.—A female, aged 37, who returned to Hospital for removal of an operable supra-clavicular gland secondary to a carcinoma of the breast, which had previously been amputated. Seven injections in all were given, rising to a maximum of 2 centigrammes, but not the slightest effect was produced beyond a soreness and swelling at the site of injection, doubtless dependent upon the amount of solid material introduced. After removal the gland was examined microscopically, and

was apparently identical in character with similar glands from patients that had not undergone Schmidt's treatment. There were in particular no signs of inflammatory reaction in or around the gland.

The 9th case was that of a man in whom nine small injections were given. Treatment was discontinued by reason of the rapidly progressing enfeeblement of the patient. After death the growth was found to be a sarcoma.

It will be seen from the cases appended above that our patients derived no benefit whatever from the Schmidt Treatment.

The cases were selected by Dr. Jossé Johnson and the injections were made by him throughout.

As has already been said above, Dr. Schmidt paid a visit to the patients, and in particular pronounced Case No. 6, Charlotte B., to be a very favourable one for treatment.

She, unfortunately, like the others, was in no way affected by it.

Not a single case shewed any reaction by rises of temperature, and it must therefore be concluded that the material is not even of diagnostic value.

Dr. Schmidt's treatment must, therefore, be placed among the great number of alleged "cancer cures" which have from time to time been announced prematurely, and have not stood the test. Many of these "cures" have proved definitely harmful. Schmidt's treatment is at least free from this condemnation except in isolated instances, for, in a word, it has not in any way modified the course of the disease.

FOUR CASES OF ENDOTHELIOMA OF THE TONGUE.

(Plate I.)

By W. S. LAZARUS-BARLOW, M.D., F.R.C.P.

According to the fundamental conception of the sub-class of the sarcomata constituted by the endotheliomata it is possible for them to occur in any position of the body, except perhaps cartilage, owing to the presence of the endothelial cell wherever there are blood-vessels or lymphatics. Nevertheless it is so general for them to be found either in or in close connection with one or other of the great serous cavities of the body that their occurrence elsewhere is apt to be overlooked. This is the more likely to be the case when we have to deal with an organ like the tongue, in which the occurrence of one particular type of new growth is so enormously preponderant as is the squamous cell carcinoma.

When one takes one particular feature and considers its presence or absence in a number of growths it frequently becomes possible to make some sort of distinction amongst the members of a group that at first seemed to be indistinguishable. Thus it is clear, after a very short consideration of the group usually included under the name of the squamous cell carcinoma, that there is a marked difference according to whether cell nests are present or not. So, too, it becomes clear that the presence of cell nests, particularly if they are present in considerable numbers, is associated with a peculiar type of epithelial cell. Further, amongst those members of the group from which cell nests are absent it is possible with a little care to distinguish two types of cells which have characters allowing them to be differentiated with fair ease from one another. It is not my purpose to enter into these questions here, but the point must be borne in mind, because it will be necessary to consider the fact when discussing

whether the cases described below are to be included amongst the endotheliomata or not.

The cases to which attention is here being directed occurred among 105 cases of malignant disease of the tongue met with in the Middlesex Hospital between the years 1900 and 1903, both inclusive. It is not difficult to convince oneself that the cases of malignant disease of the tongue, although generally of the ordinary type of squamous cell carcinoma—we have not had a single example of sarcoma of the organ during the same period—with cell nests and the great diversity of epithelial cell that characterizes it, is not invariably of this nature. The first thing that arrests attention is the absence of cell nests; from this one passes to recognition of the fact that the general arrangement and the actual characters of the cells and their nuclei in the epithelial processes are somewhat abnormal, and it is usually only after a more prolonged examination that one comes to the definite opinion that the growth with which one has to deal is not a carcinoma at all, but an endothelioma. That this should be so is the less remarkable in the case of the tongue, seeing that the endotheliomata, according to the figures given above, only constitute about four per cent. of the new growths. That they have generally been overlooked explains the fact that I have been unable to find any reference in literature to the occurrence of lingual endothelioma, although the existence of endotheliomata in the upper part of the alimentary tract, including the parotid and other salivary glands and the stomach, has been recorded in a considerable number of cases.

So far as concerns the clinical and the macroscopic characters of the four cases of endothelioma of the tongue, there is nothing to distinguish them from other cases of malignant disease of the organ. All the patients were males, and their ages were 42, 44, 51, and 61. The disease ran a fairly rapid course. Taking them in the order of their ages, the first case lasted one year from commencement to death; the second was operated upon six months after being first noticed, and the patient was subsequently lost sight of; the duration of the third case was two years, and the duration of the fourth case was about fourteen months. The infra-maxillary glands appeared to be involved in all cases, but histological examination of two glands removed a short time after the partial excision of the tongue performed in the second

case failed to demonstrate any new growth, although the glands themselves were considerably enlarged. At death the first patient was well nourished; the second had lost weight considerably at the time of his operation; the third was greatly wasted at death; concerning the fourth there is no note.

Although the number of cases is too small to base thereon any conclusions, it does not seem that there is any predilection for endothelioma to affect any particular part of the tongue. In two cases the disease commenced close to the tip, in two it occurred laterally and posteriorly. In all four cases there was a marked tendency for the growth to extend to the floor of the mouth, but as this is a tendency of lingual new growths generally it is not sufficient to connect it with any possible origin in a small salivary gland. Doubtless this tendency is explained by the looseness of the tissues in this situation. In the second case, at least shortly after the lingual operation, no metastatic growth occurred in the glands; in the fourth case metastases were noted in the liver and maxillary glands; in the first case growth was found in the mandible (extension), submaxillary glands, and liver; while in the third case nodules were present in the submaxillary glands and in the lungs. Deep erosion of the superficial portions of the growth characterized all the cases. Each of the three fatal cases was associated with the presence of other abnormalities of some part of the alimentary tract: the first presented five groups of intestinal polypi and a duodenal pouch; the second, an inguinal hernia containing 18 inches of colon; and the third, a persistent Meckel's diverticulum and an omental inguinal hernia.

Microscopically the growth has in each case been of the lymphangeiomatous type, though this in the second case was associated with a considerable amount of hæmorrhage in places and with the presence of a large number of somewhat abnormal blood-vessels, and in the second and fourth cases was, perhaps, rather of a peritheliomatous than of a definitely endotheliomatous character. It will, however, be well to give the histological features of the cases in some detail.

Case No. 1.—In this case the growth was of a distinctly adenomatous type. It consisted of a large number of alveoli of large size grouped together, and separated for the most part

by only fine strands of connective tissue. The alveoli formed blunt digital processes into the muscular tissue of the tongue, but they maintained a fairly constant position with reference to one another, so that the growing edge of the mass was not irregular, but on the contrary, regular, and bounded by a fairly regular curve. Nor was the growing edge preceded by the zone of small round cells that is so commonly seen in front of a malignant growth, or rather, the zone was very narrow, fragmentary, and ill-defined. Upon the whole, from the microscopic examination one would rather have inclined to the opinion that the growth was non-malignant. In the centre of the mass was a branching core of material that appeared to be connective tissue which had undergone a hyaline degeneration, and as it was from this central core that the fine fibrous trabeculæ passed which divided up the mass, it is clear that the entire growth was somewhat papillomatous in character.

The adenomatous masses were themselves divided up by connective tissue into smaller irregular masses, and these were filled with cells. It was characteristic of the entire growth that there was a complete absence of central degeneration in these masses of cells. The cells, too, throughout the cell processes were particularly uniform in appearance, and there was no crowding of the cells or deeper staining of their nuclei at the peripheral portions. Concerning the actual cells it is impossible to speak as fully as is desirable, for the character of the growth was not determined until all the material had been fixed and hardened, so that it was too late to examine the fresh cells in a scraping. The nuclei were of that uniform character in the matter of size and of staining that is so often seen in the case of endothelium. For the most part they were round or oval, contained but little chromatin, and shewed a tendency to concentration of the chromatic substance at the periphery and at the very centre of the nucleus. Judging from the number of the nuclei in a single alveolus and the distance between individual nuclei the cells themselves must have been of considerable size. No real difference obtained in the appearance of the alveoli or of the component cells according to the plane in which the sections were cut.

The secondary growths in the lymphatic gland and in the liver were of great interest. In the lymphatic gland the

appearances were very like those in the primary growth, with the exception that there was some evidence of a degenerative change affecting the cells in the centre of the alveoli, and a considerably greater degree of fibrosis. This fibrous tissue was densest around the individual masses of growth, and seemed to form a sort of capsule for them; from the peripheral fibrous tissue, strands of fair size passed into the metastasis itself and divided it up into a number of rounded, polyhedral, or irregular masses of various sizes. The metastasis in the liver differed considerably from both the primary growth and the metastases in the lymph glands. Although it was quite visible to the naked eye, it was easy to overlook it even with a low power of the microscope; for not only had the nodule a very irregular outline, it also consisted of very small alveoli. Few of the alveoli shewed on section more than ten or a dozen nuclei. The aggregations of cells were sometimes circular, sometimes oval, and sometimes irregular, so that it was clear that one had to do with a branching growth of which the solid processes of cells were of a much smaller size than in the primary growth. The nuclei, too, in the hepatic metastasis differed from those in the primary growth in being far more irregular in size and shape. A relatively large amount of fibrosis was also present in the hepatic nodule as in the other situations. An additional point of difference from the primary growth and the metastases in the lymphatic glands consisted in the presence of numerous aggregations of leucocytes in various positions. These leucocytes were collected outside the cell masses and in connection with the fibrous tissue trabeculæ; apparently in no instance had they penetrated into the very centres of them.

Case No. 2.—In this case the general arrangement of the masses of the tumour was very different from what obtained in the preceding case. There was no attempt at alveolation, but, on the contrary, the masses of cells spread in all directions and invaded the areolar tissue in the floor of the mouth. Here it ran particularly in the connective-tissue septa, and at the growing margin this was easily seen; more towards the centre of the growth the number of cells was so great that there persisted no longer any trace of areolar structure, but the entire section was that of an undifferentiated mass of cells. A certain amount of

young connective tissue which carried small blood-vessels divided up the masses in some degree. At one point the growth was of a definitely hæmorrhagic character, and here the cells of the growth might be seen sufficiently separate to form an opinion of their appearance. They were of fair size, possessed a relatively large amount of faintly staining protoplasm, and a round nucleus which stained poorly with hæmatoxylin. The growth shewed no sign of degeneration.

At another part of the growth the appearances were somewhat different and of a definitely peritheliomatous character. Here there were visible numerous small alveolar arrangements that had a more or less central tubular appearance, the cells being placed circumferentially and being separated from a lumen by a definite limiting membrane. At a little distance larger masses, comparable with those in the portion of growth first described, also shewed spaces, but here they were eccentric and irregular, circular, or oval in shape, and it was not certain that all of them represented central canals of vessels, as probably was the case with the more regular and far smaller alveoli that have been mentioned above. The blood-vessels themselves in the peripheral parts of the growth (probably vessels of the tongue as yet undestroyed by the tumour) seemed to be unaffected by any change of their endothelial lining, but some of the smaller vessels lying definitely within the boundaries shewed proliferation of their endothelial cells. In that portion of the growth which was of a hæmorrhagic character the appearances were somewhat those of an ordinary angeioma, though the blood spaces were much smaller than in the cavernous angeioma, while the amount of inter-vascular substance was far less than it is in the case of a capillary angeioma.

Some weeks after the primary operation two submaxillary lymphatic glands were found to be enlarged and were removed. Microscopic examination shewed that they were not the seat of new growth, but only of inflammation.

Case No. 3.—In this case alveolation was well marked, and the processes of cells were elongated and (towards the growing margin) very narrow. At the centre of the growth, where the alveoli were more spherical and far larger, there was definite central degeneration. These degenerated areas were sharply

defined from the cells of the new growth, and sometimes were separated from them by small agglomerations of cells that could not be distinguished from lymphocytes. The cells of the growth lying outside these degenerated areas and between the fine strands of connective tissue that divided up the growth were loosely packed, and were characterized by possessing a very regularly round nucleus which stained but poorly. Quite close to the periphery of the cell masses—and to some extent the same held good in the immediate neighbourhood of the areas of degeneration—the nuclei of the cells were smaller and stained more deeply. The masses of cells were quite avascular, nutrition to the growth being conveyed by the minute blood-vessels that ran in the small amount of newly-formed fibrous tissue dividing up the growth. The secondary growths in the lymphatic glands and in the lung were practically identical with the primary growth in histological appearances. Nevertheless in the case of the lung the central degeneration of the masses of cells was not confined to the centre of the metastasis, but was to be found in the cell masses right at the periphery. In the case of the lung, too, the nuclei of the cells in the peripheral masses of cells corresponded with the general compressed arrangement of these cell masses, and were elongated instead of being round.

Case No. 4.—In this case the alveolar arrangement of the masses of cells was also visible, but the collections of cells were more irregular and smaller than in the preceding cases. In places, too, the tumour was somewhat of the peritheliomatous type. As in the other cases, the essential cells of the tumour were fairly large and possessed a large round or slightly oval nucleus which contained but little chromatic substance. In those parts of the tumour where the peritheliomatous character was not marked, the cells nevertheless presented the same appearances, and there could be little doubt concerning their nature. Throughout the tumour there was no trace of an intercellular space. The small and irregular masses of cells were separated from one another by well-formed connective tissue. For the most part the cells in this connective tissue were young, as evidenced by the appearances of the nuclei. A somewhat large number of cells, which could not be distinguished from lymphocytes, were scattered throughout this connective tissue,

and at places these cells were collected into small agglomerations. Secondary growths were present in the liver and were mostly cystic, with a narrow margin of white material lining the cysts. The contents of the cysts appeared to be blood in the majority of cases, and the hepatic tissue surrounding the metastases was everywhere intensely congested. Microscopically the more central parts of the nodules were intensely cellular, and alveolation was but indistinct. Further towards the periphery the alveolation was well marked, though the alveoli were small, irregular, and narrow, and were separated from one another by only a small quantity of fibrous tissue. At the very margin of the nodule the peritheliomatous character of the growth became distinct, being shewn by the presence of circular, oval, and irregular tubules surrounded by a layer of cells with faintly staining nuclei. The resemblance between the hepatic nodules in this and the first case was considerable.

In considering the above-mentioned cases the most important point to be borne in mind is the possibility that we have not to do with endotheliomata at all, but with a specialized variety of squamous cell carcinoma. To this point short reference has already been made, but it is so important that it must be further considered.

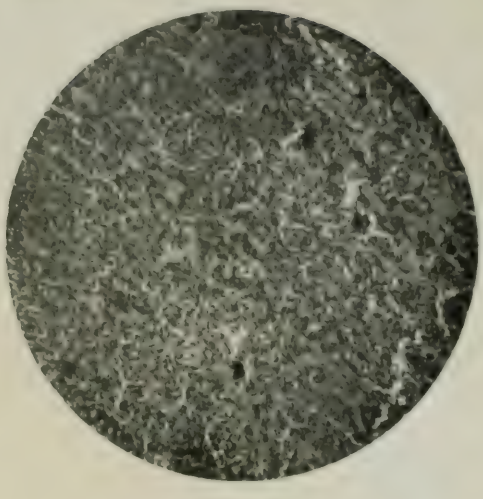
From a purely theoretical point of view it is clear that we might have a squamous cell carcinoma originating from the Malpighian layer or from the prickle cell layer of the epidermis. Whether a squamous cell carcinoma could arise from the keratinizing layer alone seems doubtful. It is also clear that even in the case of a carcinoma arising from the Malpighian layer alone we might have one variety of growth which grew rapidly, and in which the cells hardly passed beyond the undifferentiated state in which they occur in the Malpighian layer, a second in which they advanced as far as to form something akin to prickle cells, and yet a third variety in which one met with a modified Malpighian layer, a modified prickle cell layer, and a modified keratinous layer. This third variety is of frequent occurrence; indeed it forms the commonest variety of squamous cell carcinoma met with in the tongue. So far as I know, the second species ("prickle cell" carcinoma) is not recognized, but it has seemed to me that in a certain number of cases the appearances warrant such a view. In these cases one

may or may not find a peripheral layer of cells which have the characters of the germinal epithelium, but practically the entire bulk of the epithelial processes consists of cells of irregularly polyhedral shape with fairly large nuclei that stain but feebly, and very frequently shew that vacuolization or separation of the nucleus from the body of the cell that is so common an appearance in the prickle layer of normal skin. At the same time it is abundantly clear in these cases that the individual cells in the cancerous cell masses *are separated from one another by narrow clear spaces which instantly recall the spaces in normal skin across which the prickles themselves pass.* This variety of growth, too, we should *a priori* expect to meet in situations clothed with a squamous cell epithelium that does not readily undergo keratinization under normal conditions. In this connection it is noteworthy that such a large proportion of squamous cell carcinomata of the cervix uteri shew a complete absence of cell nests, as well as general appearances of the epithelium in the cell masses which differentiate them from the usual type of squamous cell carcinoma. Clearly such a type of growth might have originated from either the Malpighian or the prickle cell layer alone.

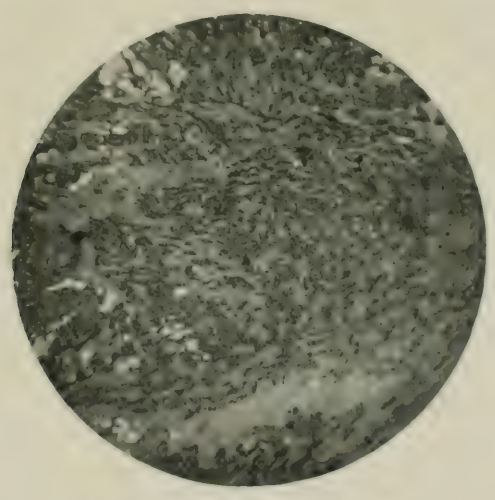
It is with regard to the cases that one can theoretically consider as possibly arising from the germinal layer of the epidermis, and as consisting of cells that hardly undergo any further differentiation, that difficulty arises. It is true that the cells of the normal Malpighian layer are approximately columnar, and possess an elongated nucleus that stains well with the ordinary nuclear dyes. But it is easy to understand that such cells when growing rapidly might become rounder and possess a round or oval nucleus that stained more faintly. Under these circumstances it would be extremely difficult to distinguish them from endothelial cells. Hence, in the cases that have been described above, it is impossible to be absolutely certain that we have not to do after all with a specialized variety of squamous cell carcinoma. In this connection the fact that two of the tumours shew, in certain parts, distinctly peritheliomatous characters seems to me to be of extreme importance, and I have, personally, little doubt that they have been rightly termed endotheliomata.

One difficulty that arises in reference to this question of

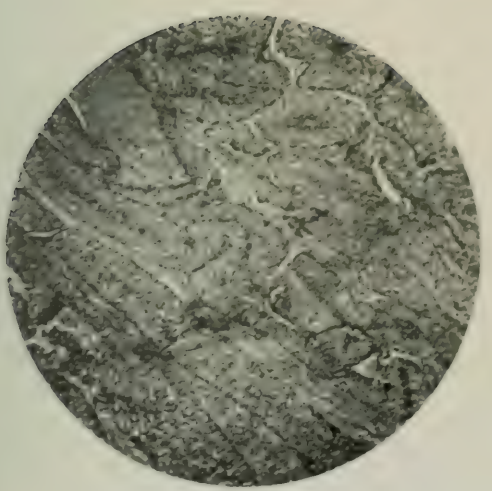
CASE 1.—TONGUE.



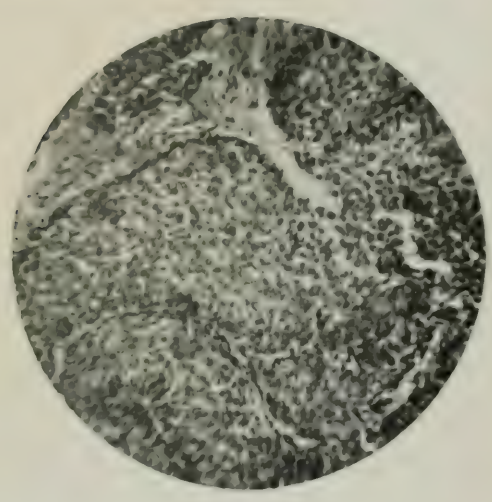
CASE 2.—TONGUE.



CASE 4.—METASTASIS IN LIVER.



CASE 3.—TONGUE.
(LOW POWER.)



CASE 3.—TONGUE.
(HIGH POWER.)

distinguishing between squamous cell carcinoma and endothelioma consists in the fact that endotheliomatous cell nests have been described (Borst). In the fourth case a small number of these cell nests were recognizable, but they offer manifest differences from the cell nests of squamous cell carcinoma, and, in addition, are but rarely found in endotheliomata. This difficulty is, therefore, not a great one.

So far as the entire question is concerned, the importance of recognizing that all cases of malignant disease of the tongue are not carcinomatous seems to me to lie in the fact that many authorities consider that the ultimate ætiology of the carcinomata and the sarcomata, with which the endotheliomata must perhaps be reckoned, is not one and the same. The resemblance of the sarcomata to many inflammatory formations may perhaps mean that the difficulty of interpreting the sarcomata and endotheliomata is not so great as the difficulty of explaining the carcinomata.

STATISTICS OF MALIGNANT DISEASE ADMITTED TO THE MAYO HOSPITAL, LAHORE, PUNJAB, INDIA.

From 1892 to 1903 inclusive.

By

DAVID W. SUTHERLAND, M.D., M.R.C.P., F.R.S. (Edin.),

capt. I.M.S., professor of medicine, lahore medical college.

The Mayo Hospital in Lahore draws its cases from all parts of the Punjab, and to a less extent from the adjacent independent States. An attempt has been made by search through the Hospital registers to gain some idea of the prevalence of malignant disease in this part of India, and the cases collected have been analyzed as far as the information available would permit.

Incidence of Malignant Disease.

The total admissions into Hospital for all diseases, during the twelve years from 1892 to 1903, were 43,412, of which 792 were cases of malignant disease. These are returned in the registers as: Carcinoma 400, Sarcoma 334, "Abdominal Tumours" 35, and "Malignant Growths" 23. It is to be regretted that no more definite information as to the nature of the two last groups can be obtained, and they are accordingly analyzed separately in the following tables wherever thought advisable. Taking all 792 to be cases of malignant disease, the proportion to other admissions works out roughly at 18 per thousand.

Varieties.

The tumours removed in Hospital were examined microscopically in the pathological laboratory of the Lahore Medical College in 226 cases, and the results shew 87 to have been forms of carcinoma and 139 varieties of sarcoma. These have been analyzed and shew as:—

(a) *Carcinoma.*

Squamous cell	Epithelioma 52, rodent ulcer 3.
Columnar cell	1
Spheroidal cell	Scirrhus 23, Encephaloid 8.

(b) *Sarcoma.*

Spindle cell	50	Alveolar	3
Fibro-sarcoma	29	Osteo-sarcoma	2
Myeloid	4	Mixed cell	10
Glio-sarcoma	2	Melanotic	7
Round cell	19	Lympho-sarcoma	3
Myxo-sarcoma	10		

Sites.

(a) *Carcinoma.*

In 329 out of the 400 cases the site of the disease was mentioned, and the results in order of frequency are:—

Penis	72	Anus	5
Skin	58	Intestines	3
Breast	50	Pancreas	3
Rectum	30	Œsophagus	2
Uterus	23	Floor of Mouth	2
Liver	23	Kidney	1
Tongue	20	Brain	1
Lip	10	Vagina	1
Bladder	6	Vulva	1
Pharynx	5	Peritoneum	1
Larynx	5		

The remainder were merely shewn as: Rodent ulcer 36, epithelioma 20, and carcinoma 15.

(b) *Sarcoma.*

The site was specified in 242 instances, and analysis of these shews :—

Head and Neck, 112.

Jaws	53	Eyelids	6
Face	13	Neck	5
Orbit	13	Lips	2
Nose	10	Scalp	1
Nasopharynx	9		

Lower Extremity, 59.

Thigh	17	Foot	7
Leg	13	Amputation Stump	2
Femur	10	Buttock	1
Knee	9		

Organs, 26.

Testicle	8	Breast	1
Parotid	5	Gums	1
Ovary	3	Rectum	1
Lymph Glands	3	Omentum	1
Tongue	2	Thyroid	1

Upper Extremity, 24.

Shoulder	7	Forearm	4
Arm	6	Hand	3
Elbow	4		

Trunk, 21.

Abdomen	7	Axilla	1
Back	7	Groin	1
Pelvic Bones	3	Scrotum	1
Chest	1		

The rest were simply returned as Sarcoma 79, and Osteo-Sarcoma 18. In the case of Abdominal Tumours and Malignant Growths no site was mentioned in the registers.

Admissions Year by Year.

In order to determine whether malignant disease is on the increase or not in this province the yearly admissions have been separated out, with the results given below. It appears from this table that the admissions year by year have been fairly uniform, and there has been no apparent increase in recent years beyond that perhaps due to improved facilities for reaching hospital.

	Total Admissions.	Carcinoma.	Sarcoma.	Abdominal Tumours.	Malignant Growths.	Totals.
1892	2379	22	19	4	0	45
1893	3759	29	18	1	1	49
1894	3548	28	21	6	0	55
1895	3896	28	25	3	0	56
1896	3703	43	31	1	0	75
1897	3787	30	43	3	0	76
1898	3347	37	38	2	1	78
1899	3458	45	29	2	1	77
1900	3788	34	28	3	4	69
1901	3871	25	27	2	4	58
1902	4008	40	28	4	6	78
1903	3868	39	27	4	6	76
	43,412	400	334	35	23	792

Race.

The race or caste was mentioned in 790 cases, but the native patients were only separated into the two head religious classes, Hindus and Mohammedans. The total admissions of Hindus and Mohammedans into Hospital are pretty even, while both are almost equally represented in the Lahore District. A glance at the result of the race analysis shews a more or less equal prevalence of malignant disease among the two peoples with one important exception. This exception obtains in the case of carcinoma, where the Hindu admissions exceed the Mohammedans by 80, a difference almost entirely due to 72 cases of epithelioma of the penis among Hindus—an affection from which Mohammedans (who practise circumcision) very rarely suffer. In the case of sarcoma the admissions for the two classes are absolutely equal.

	Carcinoma.	Sarcoma.	Abdominal Tumours.	Malignant Growths.	Totals.
Hindu - -	228	164	17	12	421
Mohammedan -	148	164	17	11	340
European -	23	4	0	0	27
Eurasian -	1	0	1	0	2
	400	332	35	23	790

A striking fact is the small number of cases among Eurasians, who make up a large proportion of the in-patients in the Albert Victor Wing of the Mayo Hospital. Only one case of carcinoma and one abdominal growth occurred out of 790 admissions for malignant disease. Twenty-seven admissions in twelve years seem also a small proportion for the European patients.*

Occupation.

Occupation in India is largely a matter of caste, especially among Hindus, and the analysis serves as a complement to the table of race statistics. The occupation was given in 500 cases, and the result shews that most occupations are liable to the affection, while the results themselves are more or less in proportion to the number of those who follow the various occupations.

The analysis is:—

Cultivator	246	Washerman	3
Shopkeeper	67	Mason	3
Labourer	32	Cook	2
Beggar	31	Tailor	2
Servant	15	Policeman	2
Carpenter	13	Watchman	2
Weaver	12	Baker	1
Sweeper	11	Teacher	1
Water-carrier	7	Bandmaster	1
Sepoy	7	Messenger	1
Blacksmith	6	Ayah	1
Clerk	6	Nurse	1
Shoemaker	5	Midwife	1
Dyer	4	Compositor	1
Pensioner	4	Gardener	1
Groom	3	Bookbinder	1
Barber	3	Pleader	1
Potter	3		

* In answer to enquiries Dr. Sutherland gave the figures for admissions of Europeans and Eurasians respectively during the three years 1900, 1902, 1903, as below:—

Year.	Europeans.	Eurasians.
1900	506	548
1902	340	482
1903	335	467

From this it appears clear that there is a far smaller incidence amongst Eurasians than amongst Europeans in India, however the figures amongst the latter may compare with the figures obtaining for Europeans at home.—Ed.

Age.

Mention was made of the age in 783 cases, and an analysis of these arranged in decades is given below. The results, however, cannot be considered very reliable, for a native seldom knows his real age. This defect is to some extent minimized by the arrangement into decades.

	Carcinoma.	Sarcoma.	Abdominal Tumours.	Malignant Growths.	Totals.
1—10	0	21	0	0	21
10—20	0	44	3	2	49
20—30	32	68	10	3	113
30—40	72	79	7	5	163
40—50	114	58	13	5	190
50—60	87	40	2	5	134
60—70	69	16	0	3	88
70—80	12	1	0	0	13
80—90	7	1	0	0	8
90—100	1	2	0	0	3
100—110	1	0	0	0	1
	395	330	35	23	783

This shews the maximum ages of prevalence as :—

Carcinoma...40—50, 114; 50—60, 87; 30—40, 72; 60—70, 69.
Sarcoma ...30—40, 79; 20—30, 68; 40—50, 58; 10—20, 44.

Sex.

Owing to the restrictions of the Caste many more males come to Hospital than females, and allowance must be made for that fact in the statistics, which for 788 cases shew as :—

	Carcinoma.	Sarcoma.	Abdominal Tumours.	Malignant Growths.	Totals.
Males -	270	255	22	18	565
Females -	126	79	13	5	223
	396	334	35	23	788

Distribution of Cases.

Analysis of the places of residence shew patients to have come from every part of the Punjab, from Kashmir and the adjoining States beyond the frontier. The number of places from which cancer patients come is so numerous that it would be tedious to mention them all in detail, hence only the figures for Lahore and the adjoining Districts are given.

Lahore	289	Gujrat	18
Gujranwalla	66	Ludhiana	15
Sialkot	47	Montgomery	12
Patiala	36	Hoshiarpur	11
Amritsar	34	Jhilum	10
Furozepore	27	Jullundur	4
Gurdaspur	22	Jammu	4

Taking the official returns from the entire Punjab, as received in the office of the Inspector General of Civil Hospitals of the Province, for the years 1899—1901, in all the Hospitals and Dispensaries, the figures were 287, 249, and 262, giving proportions to the total number of other diseases treated of ·09 per mille, ·07 per mille, and ·09 per mille respectively.

Remarks.

These statistics are too few to be of much value in themselves, but taken in conjunction with similar statistics from other parts of India they may prove useful. In themselves they tend to shew that cancer is not a common disease in the Punjab, but such cases as occur apparently affect all classes, and are more or less evenly distributed throughout the province. The comparative freedom of the Eurasian classes, which is evident in Lahore, may not be borne out by statistics from other Districts in India, but it has seemed worth calling attention to.

The carcinoma statistics quoted in this Paper bear out the general principle that cancer tends to occur at the sites of chronic irritation where there is constant need for cell repair. Fifty-eight cases of epithelioma and 36 of rodent ulcer occurred in the skin, which in India is almost constantly the seat of injury, owing to the scanty clothing worn by the Natives. Many of these are of the scalp. It seems possible that they are

set up by irritation caused by cuts with a blunt razor, for most Mohammedans shave the head as a whole, while many Hindus shave a portion. In patients from Kashmir an epithelioma of the skin of the exterior abdominal wall is common from burns produced by small charcoal fires in earthenware vessels, which they hold against the bare skin under the long, flowing skirt in winter to keep themselves warm. The freedom of Mohammedans from cancer of the penis, and their practice of circumcision, bears upon this point.

The nature of the diet does not seem to affect the incidence of cancer in the Punjab, for although both classes are for the most part vegetarians, the Mohammedans supplement this vegetable diet with meat, while the Hindus do not, yet both equally suffer from cancer. A vegetable diet makes the digestion of the Native more intestinal than gastric, and this probably throws greater strain on the pancreas, intestines, and liver than on the stomach. It is noteworthy in this connection that abdominal cancer, in Hospital practice in India, is much more common in the three former situations than in the stomach. This is probably helped by the frequent implication of these organs in tropical diseases. Alcohol also can have little relation to the disease, for Mohammedans rarely take it, while Hindus constantly indulge in various kinds of native spirits—more or less alcoholic. Syphilis, too, is equally prevalent in both classes, and is a very much more familiar disease in Hospital than cancer. There is nothing in the Punjab to shew that Malaria is in any sense related to cancer, for while malaria is the most common of all diseases, cancer is rare, and my own experience in one of the most malarial regions beyond the Punjab frontier for nearly two years gave only 4 cases of cancer to 1,640 of malaria. The spleen, too, which is always affected in malaria, is hardly ever the seat of cancer, at all events in this part of India.

LAHORE,
10th April, 1904.

MALIGNANT DISEASE IN INDIA AND IN ENGLAND.

(Remarks suggested by the Paper of Dr. D. W. Sutherland.)

By W. S. LAZARUS-BARLOW, M.D., F.R.C.P.

Insufficient as are the data from which we are at present endeavouring to deduce the incidence and natural history of malignant disease in this country and in Europe and America generally, they are even more unsatisfactory in India. And yet the merest glance at the valuable information given in Dr. Sutherland's Paper convinces one that striking differences upon the subject obtain between the experiences of medical men in India and at home.

It was owing to several long conversations with Dr. Sutherland when he was last in England that I asked him to analyze the registers of his own Hospital. Since that time I have applied to certain other gentlemen of experience in India, and am in hopes that future Reports from the Cancer Laboratories may contain the results of their investigations.

At the outset it is clear that differences are to be expected according to the different parts of India from which the reports are derived. The general climatic and racial differences are so great in the Empire that a uniformity in the incidence and type of malignant disease is hardly to be expected. Consequently it is impossible at present to predict how far the differences obtaining between the Middlesex Hospital, London, and the Mayo Hospital, Lahore, may or may not be true for England and India generally. Nevertheless, a critical examination of differences often indicates lines upon which research should in future be carried out. It is with a full recognition of the purely preliminary and tentative nature of the comparison about to be instituted that the following notes are written, but the entire subject is so vast that they may not prove valueless to others besides workers in our own Laboratories.

I.—The Limitations of Dr. Sutherland's Statistics.

It must not be considered as ungracious if a few remarks are made under this heading. For not only is Dr. Sutherland not alone responsible for the diagnoses themselves, but also he is in the main actually responsible for one of the most important parts of the Paper, viz., that which is concerned with the histological diagnoses, most of which were made by Dr. Sutherland himself when Professor of Pathology.

Dr. Sutherland has in the body of his Paper (p. 84) indicated in some measure the limitations of his figures. He refers to the relatively small number of female admissions into the Hospital, to the difficulty of the age question, to the unsatisfactory nature of the diagnoses "abdominal tumour" and "malignant disease" in a minority of the cases. Upon the whole, it will be well if we follow him in putting these two groups on one side altogether. On broad lines one might suppose that a certain number of the "abdominal tumours" would be ovarian cysts, and it is not impossible that some may be malarial and other forms of enlargement of the spleen.

But a most important difficulty arises in connection with the uncertainty whether a diagnosis has been made clinically alone or has been verified by a post-mortem examination. Thus the fact that 23 cases of carcinoma are returned as affecting the liver raises the suspicion that the disease was secondary in this region, at all events in a large proportion of the cases. So, too, the fact that out of 226 histological examinations 87 were found to be carcinoma and 139 sarcoma is susceptible of numerous explanations. Putting entirely on one side the apparently greater incidence of sarcoma in Lahore, to which reference will be made later, it is not impossible that the entire series of 226 cases has been derived from the operating theatre rather than from the post-mortem room, and that, therefore, the incidence of sarcoma is unduly high. And this suggestion is strengthened by considering that only one case of columnar cell carcinoma is noted amongst the microscopical examinations, whereas it is probable that at least the majority of the 33 cases of carcinoma of the rectum and intestines, and a certain number of the 23 cases of uterine carcinoma, were of this type.

And in the last place there comes the actual question of

diagnosis. Criticism on this point is of more than ordinary difficulty, since nothing is more certain than that experience in England is of relatively small use for practice in India. It is at least remarkable, however, from our point of view, that nine cases of sarcoma of the knee, seven of the shoulder, and four of the elbow should have occurred. In our experience the joints themselves are affected with sarcoma only with the greatest rarity. So, too, the occurrence of "sarcoma" of the scrotum (one case) and axilla (one case) raises the question as to whether they may not after all have been cases of carcinoma.

II.—Comparison between the two Sets of Statistics.

We may now turn to consideration of the statistics themselves, and for the figures pertaining to the Middlesex Hospital shall take those compiled by Mr. Hillier in the First Volume of the "Cancer Laboratory Reports" (p. 183). In this Paper 500 consecutive cases of malignant disease are analyzed, and since of this number 419 were cases of carcinoma, a good comparison with the 400 cases of carcinoma referred to by Dr. Sutherland is possible.

(A) Of the 419 Middlesex cases two-thirds (approximately) were women, while of the Mayo cases two-thirds were men. Hence it is clear that in the case of female cancer the figures of the Mayo Hospital must be doubled in order to make a comparison. Dr. Sutherland does not indicate the sex of the individual cases in his report, but since uterine and mammary carcinoma make up about three-fourths of all cancer in women (at all events in England), valuable conclusions may be drawn.

The figures are as follows:—

	Middlesex Hospital.		Mayo Hospital.	
	Number of Cases.	Percentage of total Female Cases.	Number of Cases.	Percentage of Female Cases.
Carcinoma of Female Generative Organs	78	27·96	25	19.84
Carcinoma of Breast. . .	131	46·95	50	39·68
Totals	209	74·91	75	59·52

From these figures one may fairly deduce (*a*) that in women carcinoma of the generative organs and of the breast is relatively more frequently seen at the Middlesex Hospital, and (*b*) as a corollary, that in women carcinoma of parts other than the generative organs and of the breast are relatively more frequently seen at the Mayo Hospital. The difference, too, between the actual percentages is so considerable (15·4 per cent.) that it seems probable that there is a marked difference between the districts from which each Hospital draws its female patients in respect of the regions which are attacked by carcinoma. At the same time the fact that in women breast and uterus are the chief sites of carcinoma, whether one is considering a Hospital in London or one in India, is clearly brought out.

How far error is introduced into the figures given above by inclusion of cases of carcinoma of the male breast in the Mayo series it is impossible to say. In the Middlesex series such cases have been carefully excluded. Probably, however, the error is not a considerable one, and even if present only leads to under-estimation of the differences mentioned in the text.

A further point of importance lies in the fact that whereas in the Mayo series cases of generative carcinoma are half as numerous as cases of breast carcinoma, in the Middlesex series they constitute a ten per cent. greater proportion. In view of the earlier onset of puberty, of the early marriages, and of the greater proportion of life in the East during which sexual intercourse takes place, these figures may not be without significance.

In the case of the male generative organs, the enormous preponderance of carcinoma of the penis and its occurrence almost absolutely amongst Hindus have already been referred to by Dr. Sutherland in his Paper.

In the Middlesex Hospital series six cases were met with out of 140 males, *i.e.*, 4·3 per cent. In the Mayo Hospital series there were 72 in number and constituted 26·7 per cent.* The fact itself is striking, but whether the difference between the

* The percentage is actually greater than this, for whereas 396 cases have been analyzed in the Mayo Reports according to *sex*, only 329 have been analyzed according to *site*. Probably a certain number of the balance of 67 cases were carcinoma of the penis; and if we estimate this on the figures given, an addition of 14 cases must be made, giving the percentage of penile cancer amongst males as 31·9.

great incidence in Hindus and the relative absence amongst Mohammedans is to be ascribed to the practice of circumcision by the latter is doubtful. Circumcision in this country is comparatively rare. The point is obviously one upon which further research is necessary.

(B) Passing from the consideration of cases in which the sex is certain, to those in which males and females must be grouped together, other points worthy of attention present themselves.

Dr. Sutherland has referred to the great frequency with which carcinoma of the skin has been met with at his Hospital. A comparison with the Middlesex figures brings this out even more clearly, for whereas the percentage of cutaneous carcinoma to the whole number of cases is in the Middlesex series only 3·8, in the Mayo series it is 17·6.

In the case of the alimentary tract it will be well to place the figures and percentages side by side.

CARCINOMA OF VARIOUS PARTS OF THE ALIMENTARY TRACT.

	Middlesex Hospital.		Mayo Hospital.	
	Cases.	Percentage of Total Alimentary Cases.	Cases.	Percentage of Total Alimentary Cases.
Lip, Cheek, Palate . .	20	12·9	10	9·7
Tongue and Floor of Mouth	47	30·3	22	21·4
Pharynx and Œsophagus .	8	5·1	7	6·8
Stomach	19	12·2	—	—
Intestines	7	4·5	3	2·9
Rectum	39	25·1	30	29·1
Anus	—	—	5	4·8
Liver and Bile Duct . .	6	3·9	23	22·3
Pancreas	9	5·8	3	2·9

The total number of cases affecting parts of the alimentary tract in the Middlesex series is 155, or 37 per cent. of the entire carcinomatous series. In the Mayo series it is 103, or 31·3 of the series of 329 cases in which the site is mentioned. If the absence in the Mayo series of any cases of carcinoma of the stomach is due to the facts that cancer of this viscus is usually recognized at an autopsy, and that autopsies were not usually

made,* there does not seem to be any great difference between the degrees to which the alimentary tract is involved by primary carcinoma in the two Hospitals. Nevertheless Dr. Sutherland specifically refers to the rarity of cancer of the stomach (p. 91) as compared with carcinoma of lower parts of the alimentary canal. Possibly some of the very large number of cases of hepatic cancer were really secondary to cancer of the stomach, though some were secondary to carcinoma of the intestine.* Beyond doubt, if all the hepatic cases are primary in that organ, whether in the hepatic cells or in the bile passages, we are face to face with as remarkable a liability to disease here as occurs in the case of the penis. In this connection it is worth mentioning that Dr. Sutherland informs me that in his District cirrhosis of the liver is extraordinarily prevalent. The greater preponderance of rectal and anal carcinoma at the Mayo Hospital (33·9 per cent. as against 25·1 per cent. at the Middlesex Hospital) may perhaps be explained by the harder character of the fæces, resulting from a diet mainly composed of vegetable and grain.

(C) So far as concerns the relative number of carcinomatous admissions to the general admissions into Hospital, it is impossible to compare the Mayo and the Middlesex by reason of the very large amount of cancer taken in at the latter Hospital. This appears from the fact that the Middlesex Hospital received as many cases in a little over two years as the Mayo Hospital admitted in twelve, although the total annual admissions in both Hospitals are about the same. Corresponding with this the number of cancer admissions to admissions for other diseases works out at the Middlesex at about 57 per thousand.

In another general Hospital in London where there is no special Cancer Charity, the cancer admissions are about 43 per thousand. Compared with these figures the cancer admissions at the Mayo Hospital are remarkable, for they amount to less than 10 per thousand, and amply justify Dr. Sutherland in remarking that "Cancer is not a common disease in the Punjab."

While we are considering this branch of the subject, it will be well to point to the very marked difference that obtains in the case of sarcoma.

* Dr. Sutherland writes that the diagnosis was made "in many instances" after an exploratory incision during life; in only a few instances were post-mortems made. He also reiterates his statement that "cancer of the liver is often primary."

At the Mayo Hospital sarcoma admissions amount to about 8 per thousand; at the Middlesex Hospital, where one would *a priori* expect a large number, owing to the existence of a special Cancer Charity, and to the ignorance of the public as to the difference between carcinoma and sarcoma, the sarcoma admissions are about 11 per thousand. At the other London general Hospital to which reference was made above, sarcoma admissions constitute about 8 per thousand.

How far the figures thus obtained are comparable it is difficult to say, for probably a very considerable amount of the sarcoma in London is derived from the provinces. Upon the assumption that the figures are comparable—and it is probable that the Mayo Hospital bears much the same relation to the surrounding districts as the Hospitals in London bear to the provinces—it appears that the far smaller amount of malignant disease admitted to the Mayo Hospital depends entirely upon the existence of far smaller amount of carcinoma in the districts from which it draws its patients. The incidence of sarcoma around London and around Lahore seems to be much the same.

One word of caution in accepting these conclusions is, however, necessary. There is little doubt that the Hospital accommodation per thousand of population is much higher in London and around than it is in Lahore and its neighbourhood. For this reason the Lahore statistics probably afford a less accurate estimate of the incidence of malignant new growths amongst the sick population of the Punjab generally than do the London statistics of the incidence in and around London. The figures for the Punjab may be too high or too low, but nevertheless the difference between the Lahore and the London statistics in the matter of carcinoma at least is too great for their complete explanation upon this view. There can hardly be room for doubt that carcinoma is rare in the Punjab, whatever may be the case in reference to sarcoma.

(D) Upon the question of race it is impossible for comparison to be made between the two series of statistics. Dr. Sutherland has adverted to the chief points worthy of notice in his own figures. In the absence of information over an extended period of years on the total number of general admissions of Europeans and Eurasians, it is impossible to criticize the extremely small

numbers of cases of malignant disease further than has been done as a note in Dr. Sutherland's Paper. If future investigation should confirm the relative immunity of Eurasians—and enquiries on these lines have already been commenced— we shall have at hand a positive fact of enormous importance. That such a relative immunity should obtain is not inconsistent with the generally recognized resistance of cross-breeds, whether animal or vegetable, to many varieties of disease.

(E) Age.—It will be convenient to place the Middlesex and the Mayo series in parallel columns.

Middlesex Carcinoma Series.		Mayo Carcinoma Series.	
Age.	Number of Cases.		Number of Cases.
1—10	0		0
10—20	1		0
20—30	6		32
30—40	51		72
40—50	114		114
50—60	139		87
60—70	84		69
70—80	19		12
80—90	5		7
90—100	0		1
100—110	0		1
Total..	419	Total..	395

From this it appears that the greatest incidence of carcinoma occurs ten years earlier in the Mayo Hospital series, and also that the disease is more prevalent between the ages of 20 and 40.

In view of the facts, however, (*a*) that the two sets of figures do not deal with the same years, (*b*) that the age of maximum incidence differs in various decades even within the experience of the same Hospital,* and (*c*) that in the absence of histological examination a certain number of sarcomata may be included amongst the carcinomata, it would be unsafe to draw definite conclusions.

* See Paper by W. S. Lazarus-Barlow and W. Gordon Taylor in this Volume.

CONTRIBUTION TO THE STUDY OF THE BLOOD IN MALIGNANT DISEASE WITH REFERENCE TO ITS SPECIFIC GRAVITY.

By J. J. DOUGLAS, M.D., F.R.C.P.E.,
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I.—INTRODUCTION.

The blood in malignant disease has been the subject of numerous exhaustive researches. Nevertheless they have been concerned more with the formed elements (*cf.* a Paper by Price-Jones in Vol. I. of these Reports) and hæmoglobin value than with the other constituents. In particular, among the general characters of the blood little attention appears to have been paid to its specific gravity. It was on this account that the following observations were made, and it was hoped also that possibly some variations in the specific gravity of the blood might be established, which would be of service in the early diagnosis of internal forms of the diseases in question.

According to Sherrington and Copeman [1]—and Schmaltz [2] takes practically the same view—alterations in the specific gravity of the blood may be due to one or more of the following causes:—

1. An increase or diminution in the number of corpuscles in a given volume, the specific gravity of individual corpuscles, and of the plasma remaining unchanged.

2. An increase or diminution in the density of the plasma, the specific gravity, and the number of the corpuscles remaining unchanged.

3. A simultaneous increase or diminution in density, both of the corpuscles and plasma, with or without alteration in the number of corpuscles in a given volume of the blood.

On these grounds it seemed desirable that observations should be made as regards the specific gravity, not only of the whole blood, but also of the plasma and the corpuscles, and that the relative proportions of the volumes of the two latter should be determined.

II.—PREVIOUS WORK.

With regard to previous work on the specific gravity of the blood in cancer, Cabot [3] makes the statement that "the specific gravity is reduced in most cases, running roughly parallel with the hæmoglobin," and in this connection Bierfreund's [1] observations on the regeneration of the hæmoglobin, after operations in cancer cases, are of interest, but seem to want confirmation. Grawitz [5] found that the number of the red corpuscles, the dry substance of the blood, and its specific gravity all underwent diminution with the advance of the cancer cachexia. Peiper [6] in cases of carcinoma ventriculi obtained low specific gravities. Hammerschlag [13] also, in a paper on hydræmia, gives the results of his observations on a few cancer cases. He obtained low blood specific gravities in all except a case of œsophageal growth, where the high density of the blood was attributable to the difficulty the patient had in swallowing. Here the peculiarity is probably explicable by a deficient absorption of fluid.

III.—METHOD.

The specific gravity method of Roy (Lloyd Jones) was employed, and the writer cannot understand the objection to it raised in a recent paper [7] on the grounds that it needs a relatively large amount of blood. As pointed out by Jones [8] in his original paper, quite a small drop suffices. A series of solutions of varying specific gravity were made up from 1·0200 to 1·0920. These were prepared with glycerine and distilled water, and a little formalin was added as a preservative against moulds. Those above 1·0500 were estimated by means of Kew-tested hydrometers. From solutions so made those below 1·0500 were prepared according to the equation:

$$x = \frac{a\ (s' - s)}{1000 - s'}$$

When s = sp. gr. glycerine solution;
a = amount in c.cm. of ditto;
s' = sp. gr. of desired glycerine solution;
x = amount of water in c.cm. to be added.

The value of this equation was repeatedly tested, and it was found to give accurate results.

After three months the solutions were examined by the sp. gr. bottle. The specific gravity of the lower half of the series was found to have undergone very little change, the difference ranging from ·0001 to ·0003. Higher in the series, however, a distinct gain in specific gravity was found to have taken place. This was most marked in the heaviest solutions from 1·0840 to 1·0920, where the gain was as much as ·0010, and in one case nearly ·0020.* In the tabulated readings, therefore, of the corpuscular densities it should be borne in mind that the specific gravity was *at least* the figure recorded.

The blood to be examined was taken from the finger, usually the middle finger, and always between 3 and 3.30 p.m., this being a time, nearly three hours after a meal, when the quantity of fluid present in the tissues would be probably at a minimum. As a further precaution against the admixture of the blood with tissue lymph the method of Oliver ([9]) was employed as follows: Three stout rubber rings were rolled with pressure in succession, from the tip of the finger upwards, to beyond the interphalangeal joints; a piece of brass tubing was then slipped on the finger up to the rings, and the latter removed by rolling them off the finger on the tube. The puncture was then quickly made, and the first drop of blood taken for its specific gravity. This was estimated in the usual way by means of a capillary pipette, bent to a right angle a few mm. from the end, and a row of specimen tubes 2 cm. in diameter, containing the solutions. A portion of blood was then taken for the separate estimation of the corpuscles and plasma in the following way: A 2 per cent. solution of potassium oxalate was made, and, for a reason to be explained later, was coloured with a trace of solid methylene blue. This solution was found to have a specific gravity of 1·0120. By means of a pipette—that devised by Nabarro ([10]) for use in the typhoid serum test was found useful —5 c.mm. of this solution was taken up and then 45 c.mm. of blood, the whole being then drawn into the mixing bulb and thoroughly mixed. This gave a ·2 per cent. solution of potassium oxalate in blood, and efficiently prevented coagulation. The blood was then blown out into a capillary tube of approximately

* Three months later the solutions were again tested, and were not found to have undergone any noteworthy change.

uniform calibre, and centrifugalized until, by measurement, the corpuscular volume remained constant. This was found to take about four minutes. The relative volumes of the corpuscles and of the plasma were then measured, and the percentage calculated. The writer gives the figures so obtained with diffidence, being aware of the possible fallacies of such methods of volume estimation—see Biernacki ([11]), Goldsmith ([17])—and only claims for them approximate accuracy. The tube was then cut at the junction of the corpuscles and plasma, and a little of the lowest of the pasty corpuscular mass was sucked up into a capillary pipette, and its specific gravity, by Roy's method, estimated. The specific gravity of the oxalate plasma was then taken in the same way, and it was in this that the value of the blue coloration of the oxalate solution was evident. The plasma sometimes, especially if of low specific gravity, is so nearly colourless that it is very difficult to distinguish it from the glycerine solution. The methylene blue entirely removes this difficulty. The hæmoglobin was then estimated by means of Haldane's hæmoglobinometer. Finally the specific gravity of the blood was taken a second time to estimate the "lymph difference" (Oliver). This, however, presumably for the reason already stated, *i.e.*, because the blood was taken three hours after a meal, was seldom of importance. The whole time occupied in obtaining the blood amounted to scarcely more than two minutes, and one puncture was nearly always sufficient.

To correct for the addition of the oxalate solution, as far as the plasma was concerned, was simple, the dilution being merely one in ten. For the corpuscles it seemed that the following might give more accurate results. Bunge ([12]) has concluded, from estimation of the contained sodium, that, after centrifugalizing defibrinated pig's blood, the corpuscular paste still contains one-seventh of its bulk of serum. The correction of the figure with regard to the corpuscles was made on this basis, a one in seven dilution with the oxalate plasma being assumed. At any rate, it may confidently be asserted that there is an appreciable amount of plasma, even with the thickest corpuscular paste. One has only to examine a little of such a paste beneath the microscope to be convinced of the fact

IV.—RESULTS OF OBSERVATIONS.

Observations were made in 44 cases of undoubted cancer, and the results have been tabulated. Table I. gives a summary of the results in those cases in which more than one observation was made. Table III. includes those in which only a single observation was found possible. The protocols of the entire investigations from which Table I. is drawn up is given in Table II. at the end of the Paper.

Table I.—Summary of Results in Cases where more than One Observation was made.

Case.	Sp. gr. of Blood.	Sp. gr. of Corpuscles.	Sp. gr. of Plasma.	Percentage volume of Corpuscles.
I.	Fall	Rise	Fall	Fall
II.	Fall	Fall	Fall	Fall
	Fall	Rise	Fall	Rise
III.	Fall	Rise	Fall	Fall
	Fall	Fall	Fall	Fall
IV.	Stationary	Stationary	Fall	Rise
	Fall	Fall	Stationary	Fall
V.	Fall	Rise	Fall	Fall
VI.	Fall	Rise	Stationary	Fall
	Fall	Fall	Stationary	Rise
	Fall	Fall	Fall	Fall
VII.	Fall	Fall	Fall	Fall
VIII.	Stationary	Fall	Fall	Rise
IX.	Rise	Stationary	Stationary	Rise
X.	Fall	Rise	Fall	Fall
XI.	Fall	Fall	Stationary	Fall
XII.	Fall	Fall	Fall	Fall
XIII.	Fall	Fall	Stationary	Fall

If, as is generally allowed, the average specific gravity of normal blood be taken as 1·0590 for men and 1·0560 for women, it will be seen from the cases examined that in carcinoma it was markedly subnormal, being 1·0522 and 1·0481 respectively.

In several of the cases the blood in respect to specific gravity, hæmoglobin percentage, and corpuscular count will be seen to be almost or quite up to the healthy normal. See, for example, Cases 3, 7, 9, 20, 22, three of which were of mammary, and two of uterine cancer. All of these cases were of long standing, and it must not therefore be supposed that the blood examinations were made at a time before which it is possible for blood changes to occur.

Among the female cases which had a blood specific gravity of 1·0500 and over, there were:—

8	out of a total number of			10 mammary cases.
9	„	„	„	18 uterine cases.
2	„	„	„	2 rectal cases.
1	„	„	„	1 pharyngeal case.

In the remainder of these female cases the blood specific gravity was under 1·0500.

The blood specific gravity seemed to have a distinct relationship with the emaciation and general cachexia of the patient, being higher in the non-emaciating cases and lower in those rapidly wasting. It is probably in part fortuitous that rapid wasting was found more frequently among the uterine than among the mammary cases in the series investigated.

With regard to the specific gravity of the red blood corpuscles, there is a considerable divergence of opinion among the few observers who have worked at this subject. C. Schmidt [14] estimates the normal specific gravity as 1·0880—1·0889, adding that in dropsy it sinks to 1·0819, and in cholera rises to 1·1027. Welcker [15], on the other hand, gives a much higher estimate, viz., 1·1050. The writer obtained results midway between those of Schmidt and Welcker, his average in cancer cases being 1·1007 for men, and 1·0985 for women. The average obtained from the blood of nine healthy men was practically the same, viz., 1·1006. In some of the latter the corpuscular specific gravity was estimated, both by the method already indicated and by the pycnometer, the results being practically identical. While thus the average corpuscular specific gravity did not deviate very extensively from the normal, in some cases it was considerably lower (for example, in Cases 2, 6, 15, and 18); this lowering was associated in all cases with emaciation and grave cachexia.

The specific gravity of normal plasma being taken as 1·029—32 for both sexes, the density of the plasma also was found in the cases examined to be below the average, being 1·0253 for men, and 1·0271 for women. The explanation of the greater lowering in men may be the comparative rarity of the non-emaciating type of cancer in the male series. This agrees with the results of Hammerschlag [13], who finds that both in tuberculosis and in malignant disease the specific gravity of the plasma is only lowered when cachexia has become well marked. Partly, however, it may depend in both cases upon the not unnatural supposition that the effect of confining a man within the walls of a Hospital is greater than that of confining a woman, by reason of the general difference of their associations in health.

Table I. gives a summary of the results of two or more observations on thirteen cases. It will be seen that in eleven the blood specific gravity has fallen. In one it has remained unchanged, and in one it has risen. The two latter cases are those of well-nourished women of 73 and 76, with slowly growing mammary cancer. In the other cases the fall in specific gravity appears to have run parallel with the progress of the cachexia, not only in direction, but also in degree.

Another striking point is the fall in specific gravity of the plasma. In ten of the thirteen cases it is lower, in three it is unaltered, and in none is it increased.

The change in the corpuscular specific gravity is variable, but it more frequently undergoes diminution. The same may be said of the corpuscular volume.

It will be seen in the thirteen cases that the alterations in specific gravity of the blood fall under Sherrington and Copeman's headings, already referred to, as follows:—

Under the first heading . .	1
,, second heading . .	1
,, third heading . .	11

That is to say, the most frequent physical explanation of the fall in blood specific gravity is found to be a lowering of the specific gravity of the plasma, which, since it is impossible to regard it as due to a positive addition of water, must almost certainly be regarded as due to loss of solids, presumably

TABLE II.

No.	Reference.	Sex.	Age.	Disease.	Date.	Sp. Gr. Blood.	Sp. Gr. Corpuscles.		Sp. Gr. Plasma.		Vol. °/₀ Corpuscles.	Vol. °/₀ Plasma.	Hæmogl. °/₀	Period.	Difference.			
							Uncorrected.	Corrected.	Uncorrected.	Corrected.					Sp. Gr. Blood.	Sp. Gr. Corpuscles.	Sp. Gr. Plasma.	Vol. °/₀ Corpuscles.
1	C.R. 88	F.	69	C. Mammæ -	14 x. '03	1·0460	1·0870	1·0972	1·0255	1·0270	32·1	67·9	..	..	..	..	..	..
	,,	,,	,,	,, -	25 iv. '04	1·0430	1·0880	1·0985	1·0250	1·0263	30·4	69·6	..	6 mts.	— ·0030	+ ·0013	— ·0007	— 1·7
2	C.R. 490	F.	42	C. Uteri - -	15 x. '03	1·0440	1·0850	1·0944	1·0285	1·0303	30·7	69·3	..	..	..	..	..	..
	,,	,,	,,	,, - -	24 xi. '03	1·0400	1·0840	1·0936	1·0260	1·0275	24·4	75.6	46	1½ mts.	— ·0040	— ·0008	— ·0028	— 6·3
	,,	,,	,,	,, - -	26 iv. '04	1·0320	1·0840	1·0945	1·0210	1·0220	28·2	71·8	..	5 mts.	— ·0080	+ ·0009	— ·0055	+ 3·8
3	C.R. 508	F.	61	C. Mammæ -	15 x. '03	1·0540	1·0880	1·0982	1·0265	1·0281	42·8	57·2	..	..	..	..	..	..
	,,	,,	,,	,, -	21 xi. '03	1·0520	1·0920	1·1030	1·0255	1·0270	36·1	63·9	81	1½ mts.	— ·0020	+ ·0048	— ·0011	— 6·7
	,,	,,	,,	,, -	26 iv. '04	1·0510	1·0905	1·1014	1·0250	1·0263	35·1	64·9	..	5 mts.	— ·0010	— ·0016	— ·0007	— 1·0
4	C.R. 458	F.	40	C. Uteri - -	15 x. '03	1·0510	1·0910	1·1020	1·0250	1·0263	35·5	64·5	..	..	..	..	..	..
	,,	,,	,,	,, - -	2 xii. '03	1·0510	1·0910	1·1020	1·0245	1·0259	35·6	64·4	72	1⅞ mts.	Nil.	Nil.	— ·0004	+ 0·1
	,,	,,	,,	,, - -	25 iv. '04	1·0490	1·0900	1·1009	1·0245	1·0259	29·0	71·0	..	5 mts.	— ·0020	— ·0011	Nil.	— 6·6
5	C.R. 522	F.	33	C. Uteri - -	19 x. '03	1·0540	1·0860	1·0955	1·0290	1·0309	40·5	59·5	..	..	..	..	..	..
	,,	,,	,,	,, - -	23 xi. '03	1·0500	1·0910	1·1022	1·0235	1·0247	34·8	65·2	72	1 mt.	— ·0040	+ ·0067	— ·0062	— 5·7
6	C.R. 498	F.	31	C. Uteri - -	20 x. '03	1·0410	1·0810	1·0908	1·0220	1·0231	28·5	75·5	..	..	..	..	..	..
	,,	,,	,,	,, - -	23 xi. '03	1·0320	1·0850	1·0955	1·0220	1·0231	13·5	86·5	18	1 mt.	— ·0090	+ ·0047	Nil.	— 15·0
	,,	,,	,,	,, - -	25 xi. '03	1·0315	1·0840	1·0943	1·0220	1·0231	16·1	83·9	26	2 days.	— ·0005	— ·0012	Nil.	+ 3·4
	,,	,,	,,	,, - -	25 iv. '04	1·0300	1·0820	1·0922	1·0210	1·0220	14·4	85·6	..	5 mts.	— ·0015	— ·0021	— ·0011	— 1·7
7	C.R. 198	F.	74	C. Mammæ -	4 xi. '03	1·0560	1·0920	1·1029	1·0265	1·0281	45·0	55·0	96	..	..	..	..	..
	,,	,,	,,	,, -	25 iv. '04	1·0520	1·0910	1·1018	1·0260	1·0275	41·0	59·0	..	6 mts.	— ·0040	— ·0011	— ·0006	— 4·0
8	C.R. S.A.J.	F.	76	C. Uteri - -	13 xi. '03	1·0500	1·0920	1·1031	1·0250	1·0263	33·8	66·2	76	..	..	..	..	..
		,,	,,	,, - -	25 iv. '04	1·0500	1·0910	1·1021	1·0245	1·0259	34·2	65·8	..	5½ mts.	Nil.	— ·0010	— ·0004	+ 0·4
9	C.R. 345	F.	73	C. Mammæ -	24 xi. '03	1·0530	1·0900	1·1006	1·0260	1·0275	35·5	64·5	86	..	..	..	..	..
	,,	,,	,,	,, -	26 iv. '04	1·0550	1·0900	1·1006	1·0260	1·0275	36·1	63·9	..	5 mts.	+ ·0020	Nil.	Nil.	+ 0·6
10	C.R. 531	F.	44	C. Uteri - -	25 xi. '03	1·0530	1·0890	1·0993	1·0270	1·0286	37·0	63·0	68	..	..	..	..	..
	,,	,,	,,	,, - -	2 xii. '03	1·0520	1·0890	1·0995	1·0230	1·0275	33·3	66·7	72	1 wk.	— ·0010	+ ·0002	— ·0011	— 3·7
11	C.R. 502	M.	55	C. Linguæ -	4 i. '04	1·0530	1·0890	1·1000	1·0230	1·0242	28·0	72·0	55	..	..	..	..	..
	,,	,,	,,	,, -	5 v. '04	1·0440	1·0880	1·0990	1·0230	1·0242	26·7	73·3	..	4 mts.	— ·0090	— ·0010	Nil.	— 1·3
12	C.R. 496	M.	72	C. Recti - -	8 i. '04	1·0550	1·0920	1·1028	1·0270	1·0286	39·4	60·6	72	..	..	..	..	..
	,,	,,	,,	,, - -	5 v. '04	1·0510	1·0900	1·1008	1·0250	1·0263	32·5	67·5	..	4 mts.	— ·0040	— ·0020	— ·0023	— 6·9
13	C.R. 556	M.	61	C. Buccæ - -	26 i. '04	1·0600	1·0920	1·1031	1·0250	1·0263	42·5	57·5	78	..	..	..	..	..
	,,	,,	,,	,, - -	5 v. '04	1·0550	1·0900	1·1008	1·0250	1·0263	37·6	62·4	..	3¼ mts.	— ·0050	— ·0023	Nil.	— 4·9

TABLE II.

Gr.	Vol. % Corpuscles.	REMARKS.	CLINICAL REMARKS.
007	— 1·7	Lessening of blood density due to diminution of sp. gr. of plasma as well as of the % volume of corpuscles, although the sp. gr. of the latter is increased.	Disease of at least five years' duration. Growth ulcerating and bleeding. Slight fever. Patient getting very feeble.
028	— 6·3	During first period loss in blood density caused by diminution of plasma sp. gr. and of % corpuscular volume and also by slight decrease in corpuscular sp. gr. During the second period it is due solely to loss in plasma sp. gr., which is relatively great, there being increase both in corpuscular density and percentage volume.	Disease first noticed in May '02. Ulceration and hemorrhage. No fever. Patient has been rapidly emaciating lately.
055	+ 3·8		
011	— 6·7	Diminution of blood density during first period due to fall in plasma sp. gr. and in % corpuscular volume, the corpuscular sp. gr. being considerably raised. In the second period both plasma and corpuscular density have decreased, and the % corpuscular volume has become further lessened.	Growth first noticed four years ago. Breast amputated three years ago. Recurrence in axillary glands. Ulceration. Secondary deposits in viscera. No fever. Patient well nourished.
007	— 1·0		
004	+ 0·1	During first period in this case the blood sp. gr. has remained the same. The density of the plasma is diminished, but there is slight increase of the % corpuscular volume. During second period fall in blood sp. gr. caused chiefly by decrease in the corpuscular volume, though there is also a lessening of corpuscular sp. gr. Plasma density is unchanged.	Disease began two years ago. Rapid growth. No fever. Patient fairly well nourished. Slight but frequent hemorrhage.
l.	— 6·6		
062	— 5·7	Fall in plasma sp. gr., with decrease of the corpuscular % volume has caused fall of blood sp. gr. in spite of rise in corpuscular sp. gr.	Disease of four years' duration. Foul discharge. Patient well nourished. Death 14 April '04.
l.	— 15·0	During the first and second periods, which may be taken as one, loss in the blood sp. gr. seems dependant on diminution of the % corpuscular volume, which is considerable. The corpuscular sp. gr., however, is raised, and that of the plasma is unchanged. During third period there is a further diminution in corpuscular volume, and a loss of sp. gr. of both corpuscles and plasma.	Disease first noticed June '02. Offensive discharge. Recto-vaginal and vesico-vaginal fistulæ. No hemorrhage. Considerable fever. Great emaciation. Death 15 June '04.
l.	+ 3·4		
011	— 1·7		
006	— 4·0	Blood sp. gr. lowered by loss of density of plasma and also of corpuscles, with diminution of % volume of the latter.	No fever. Patient not emaciated. General conditions fair.
004	+ 0·4	The sp. gr. of the blood is unchanged in spite of slight fall in sp. gr. of both plasma and corpuscles, this being compensated by increase in % volume of the latter.	A very slow-growing case. Patient fairly well nourished. Has been in hospital four years.
l.	+ 0·6	The only case in which the blood sp. gr. is increased. This is apparently due solely to gain in % volume of corpuscles.	A slow-growing case. Patient's general condition good. No fever. No ulceration.
011	— 3·7	Fall in blood sp. gr. due to lessening of plasma sp. gr. and of corpuscular % volume. The corpuscular density, however, is slightly raised.	Disease first noticed two years ago. Hemorrhage. Emaciation. Fever.
l.	— 1·3	Fall in blood density due to loss of corpuscular sp. gr. of % volume. The sp. gr. of the plasma remaining unchanged.	Secondary growths. Disease of 18 months' duration. Patient has got very much worse during the last three months.
023	— 6·9	Diminution of blood sp. gr. caused by fall in plasma sp. gr. and in corpuscular sp. gr. and % volume.	Disease of two years' duration. Left inguinal colotomy.
il.	— 4·9	Loss in blood sp. gr. due to diminution of corpuscular density and % volume. The sp. gr. of the plasma is unchanged.	Disease of eighteen months' duration. Extension to lower jaw. Perforation of cheek. Death 2 June '04.

No.	Reference.	Sex.	Age.	Disease.	Date.	Sp. Gr. Blood.	Sp. Gr. Corpuscles.		Sp. Gr. Plasma.	
							Uncorrected.	Corrected.	Uncorrected.	Corrected.
14	C.R. 427	F.	57	C. Uteri - -	21 x. '03	1·0490	1·0870	1·0976	1·0265	1·0281
15	C.R. 482	F.	40	C. Uteri - -	13 x. '03	1·0440	1·0850	1·0950	1·0245	1·0259
16	C.R. 346	F.	58	C. Mammarum	14 x. '03	1·0540	1·0890	..	1·0250	1·0263
17	C.R. 523	F.	64	C. Ventriculi	21 x. '03	1·0460	1·0890	1·0996	1·0250	1·0263
18	C.R. 465	F.	58	C. Mammæ -	20 x. '03	1·0430	1·0760	1·0850	1·0220	1·0231
19	C.R. 454	F.	58	C. Uteri - -	27 x. '03	1·0480	1·0890	1·0977	1·0245	1·0259
20	C.R. 506	F.	55	C. Uteri - -	28 x. '03	1·0500	1·0900	1·1006	1·0260	1·0275
21	C.R. 464	F.	37	C. Uteri - -	29 x. '03	1·0500	1·0895	1·0998	1·0275	1·0292
22	C.R. 436	F.	47	C. Uteri - -	30 x. '03	1·0560	1·0890	1·0993	1·0270	1·0286
23	C.R. 485	F.	47	C. Mammæ -	2 xi. '03	1·0500	1·0900	1·1006	1·0260	1·0275
24	C.R. 481	F.	63	C. Mammæ -	5 xi. '03	1·0520	1·0890	1·0997	1·0245	1·0259
25	C.R. 415	F.	50	C. Recti - -	5 xi. '03	1·0570	1·0920	1·1020	1·0320	1·0342
26	C.R. 479	F.	65	C. Recti - -	6 xi. '03	1·0530	1·0910	1·1016	1·0270	1·0286
27	C.R. 441	F.	57	C. Uteri - -	6 xi. '03	1·0550	1·0900	1·1006	1·0260	1·0275
28	C.R. 397	F.	58	C. Uteri - -	6 xi. '03	1·0440	1·0880	1·0984	1·0250	1·0263
29	C.R. 255	F.	30	S. Femoris -	6 xi. '03	1·0490	1·0860	1·0970	1·0200	1·0208
30	C.R. 516	F.	25	C. Uteri - -	9 xi. '03	1·0510	1·0920	1·1021	1·0265	1·0281
31	C.R. 412	F.	51	C. Uteri - -	9 xi. '03	1·0420	1·0870	1·0974	1·0245	1·0259
32	C.R. 525	F.	43	C. Uteri - -	11 xi. '03	1·0420	1·0860	1·0962	1·0240	1·0253
33	C.R. 492	F.	39	C. Mammæ -	11 xi. '03	1·0505	1·0860	1·0961	1·0250	1·0263
34	C.R. 530	F.	59	C. Mammæ -	13 xi. '03	1·0560	1·0920	1·1026	1·0280	1·0297
35	B.P.	F.	39	C. Pharyngis	14 xi. '03	1·0560	1·0900	1·1003	1·0280	1·0297
36	C.R. 539	M.	52	C. Recti - -	4 i. '04	1·0510	1·0910	1·1020	1·0250	1·0263
37	C.R. 528	M.	47	C. Linguæ -	4 i. '04	1·0410	1·0910	1·1024	1·0220	1·0231
38	C.R. 547	M.	61	C. Laryngis -	8 i. '04	1·0560	1·0910	1·1020	1·0250	1·0263
39	C.R. 499	M.	84	C. Labii - -	8 i. '04	1·0530	1·0900	1·1010	1·0240	1·0253
40	C.R. 542	M.	55	Lympho-Sarcoma Cervicis	12 i. '04	1·0540	1·0880	1·0988	1·0230	1·0242
41	C.R. 523	M.	40	C. Coli - -	12 i. '04	1·0550	1·0880	1·0990	1·0220	1·0231
42	C.R. 529	M.	57	C. Linguæ -	12 i. '04	1·0510	1·0860	1·0966	1·0220	1·0231
43	C.R. 564	M.	53	C. Scroti - -	17 ii. '04	1·0540	1·0910	1·1020	1·0250	1·0263
44	C.R. 566	M.	62	C. Labii - -	22 ii. '04	1·0530	1·0900	1·1007	1·0255	1·0270

% Vol. Corpuscles.	% Vol. Plasma.	% Hb.	REMARKS.
35·5	64·5	48	Disease of twelve months' duration. General condition fair. Died suddenly 10 February '04. Jaundice.
29·4	70·6	..	Patient very cachectic and ill. Died 7 November '03. Secondary growths lung and glands.
41·2	58·8	..	Growth of very slow growth. Little emaciation.
32·0	68·0	..	Much emaciation. Died 18 December '03.
37·5	62·5	..	Disease of three-and-a-half years' duration. Secondary cervical glands. Died 16 January '04.
33·0	67·0	64	Rapid emaciation. Died 14 February '04.
32·6	67·4	78	Disease of two years' duration. Patient well nourished. R.B.C. = 5,000,000.
29·4	70·6	64	Disease first noticed two years ago. Ulceration. Hæmorrhage. Fever. R.B.C. 5,055,000.
42·2	57·8	89	R.B.C. 5,385,000
41·5	58·5	74	R.B.C. 4,720,000. Died 22 December '03.
34·8	65·8	72	Disease first noticed two years ago. Emaciation. Ulceration. Hæmorrhage. Well nourished. Died 16 March '04.
34·0	66·0	70	Inguinal colotomy 1900. Ulceration. Emaciation. Died 3 May '04.
34·7	65·3	74	
34·0	66·0	74	
36·6	63·4	64	Began two years ago. Rapid extension in mesenteric glands. Emaciation Died 2 February '04.
34·4	65·6	58	
31·0	69·0	70	
21·2	78·8	44	Died 2 February '04.
31·0	69·0	50	Died 30 November '03.
36·5	63·5	62	Died 4 December '03.
42·3	57·7	92	Died 19 January '04.
40·0	60·0	74	Disease of four-and-a-half years' duration. Secondary cervical glands.
31·1	65·9	62	Excision of rectum October '03. Recurrence. Ulceration. Hæmorrhage. Fever. Died 12 March '04.
28·5	71·5	54	Secondary cervical glands. Died 6 January '04.
..	..	66	Died 14 February '04. No emaciation. Secondary growths in thyroid and cervical glands.
35·1	64·9	64	Secondary glands. Twelve months' duration. Died 13 February '04.
40·2	59·8	62	Disease of seven months' duration. Ulceration and much cachexia. Died 7 April '04.
38·5	61·5	68	Disease of two-and-a-half years' duration. Colotomy. Patient weak and somewhat emaciated.
36·5	63·5	63	Secondary growths in neck. Died 24 January '04.
40·4	59·6	72	Inguinal glands involved. Rapid ulceration. Fever. Died 27 October '03.
..	..	..	Disease of fourteen months' duration. Died 26 June '04.

proteid, *plus* diminution in corpuscular volume, due to actual destruction or deficient formation of blood corpuscles. This accords well with an analysis made by Broca ([16]) of the blood in a case of pyloric cancer with secondary growth in the liver, of which the following are the details :—

	Case.	Normal.	Difference.
Water . . .	887·2	791	+96·2
Fibrine . .	3	3	0
Free proteid . .	55·1	68	−12·9
Corpuscles . .	45·8	127	−81·2
Salts, etc. . .	8·9	11	−2·1
	1000·0	1000·0	

CONCLUSIONS.

The writer is fully aware of the danger in generalizing from a small number of cases, but from the uniformity of the results the following conclusions appear justifiable. Further, since all the cases except two are cases of carcinoma, the conclusions are strictly applicable to that form of malignant disease alone. Whether they hold good for sarcoma must be determined by a separate research.

1. In carcinoma the specific gravity of the blood is lowered. The only exceptions to this statement have occurred in cases unaccompanied by emaciation.

2. The fall in specific gravity varies directly with the cachexia. In some measure it is a minor indication of the degree of cachexia, and therefore its estimation has a certain prognostic value.

3. The specific gravity of the blood plasma falls in carcinoma, and the fall varies directly with the degree of cachexia.

4. The specific gravity of the blood corpuscles does not, in carcinoma, vary greatly from the normal, though a fall is observed where cachexia is extreme.

5. The specific gravity of the red blood corpuscles in health is about 1·1006.

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A CASE OF SECONDARY CARCINOMATOUS DEPOSIT IN BONE, WITH ESPECIAL REFERENCE TO THE VASCULAR SUPPLY OF THE METASTASES.

(Plates II.—IV.)

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The following case is an example of a condition which, though not rare, has received very little attention from the point of view from which it will be considered in the following pages.*

A female subject who was certified to have died, at the age of 63, from "cancer of the breast," was received, in September 1901, at the Anatomical Department of the Middlesex Hospital Medical School. The patient had been admitted into the Infirmary, whence the body was obtained, one year previous to her death, with inoperable scirrhus of the breast. She had also suffered from pains in the hips and thighs, which were attributed to sciatica. There was no record of any operation having been performed before admission. The conditions found "post mortem" were the following: There was a large ulcerating tumour of the left breast, and the axillary glands were affected so that the ordinary naked eye appearances of an advanced scirrhous cancer of the breast were present. I accordingly removed the whole mass when preparing the body for the dissecting room. The thighs and knees were fixed in a position of semiflexion, and were bent over to the left side. At a later date during the course of dissection it was discovered that there was extensive secondary disease of the bones, affecting the vault of the skull, the right clavicle, some of the ribs, both innominate, and both thigh bones.

* From another and a very different aspect carcinomatous deposits in bone are discussed by Mr. Handley in the present Volume (p. 27).—Editor.

The naked eye appearances of the metastatic deposits in the vault of the skull are well seen in Plates II. and III., both of which shew that the deposits had taken place along the course of the branches of the right and left middle meningeal arteries. The skull opposite the centre of the larger deposits was increased in thickness by about one-third of an inch, both the pericranium and the dura mater being raised above the level of the surrounding bone. The scalp superficially, however, and the arachnoid membrane beneath, were quite unaffected. The calcareous portion of the bone, where the secondary deposits had occurred, was entirely absorbed, so that it was easy to pass the blade of a scalpel through the whole thickness of the skull, and remove portions for microscopic examination; moreover, on making pressure over the affected areas, the skull was felt to be soft and yielding. The parts in which the new growth had taken place were not everywhere continuous with one another, there being several isolated circular ovoid patches of growth in the position of the terminal branches of the arteries. The sagittal, lambdoid, and coronal sutures were almost entirely obliterated, and some of the cancerous deposits involved the bone in the lines of these sutures. On the outer surface of the skull tortuous injected arteries could be seen to emerge from the vault and ramify in the pericranium covering the tumour. The positions of these vessels corresponded to those of branches of the middle meningeal arteries on the inner aspect of the skull (Plate III.). These vessels were most conspicuous in the central portions and at the growing margins of the deposits; numerous minute vessels (not shewn in the drawings) could be seen also in the pericranium covering the unaffected parts of the bone between and around the secondary growths. On examining transverse sections of the skull opposite the terminal branches of the middle meningeal artery, and where the metastases were smallest, the deposits appeared to have occurred first, either in the dura mater itself or in the bone lying immediately external to it. Thence they spread to the diploë and then secondarily involved the outer table. This was apparently the general course of events; but in some places the growth seemed to have spread either by continuity along the diploic tissue, or by the formation of independent centres in this tissue, and the secondary implication of both the inner and the outer tables.

The margins of the growth were everywhere well defined, a sharp line of demarcation separating the tumour from the surrounding bone. The pericranium, however, for the distance of about one-sixth to one-third of an inch from the edge of the tumour, was thickened and more vascular than normal.

The cut surface of the tumour was smooth, of a bluish-white colour, and slightly translucent, but immediately beneath the periosteum, and scattered through the substance of the growth, there were irregular opaque patches of a yellowish-white colour, which gave to the whole surface a somewhat mottled appearance. These patches contained calcareous particles which were, apparently, unabsorbed portions of the original bone. The secondary growth, though not so dense as the primary cancer of the breast, was firm and elastic, and of fairly uniform consistence. The cut edges of the pericranium and dura mater appeared sharply marked off from the substance of the growth beneath, although they were both strongly adherent to it, and could not be torn off without removing fragments of the subjacent tissue.

The innominate bones, some of the ribs, the right clavicle, and both femora were also the seat of metastatic deposits. The appearance of the secondary growth in the innominate bones and in the ribs was very similar to that in the skull. In the case of the ilia the same complete decalcification of the bone had taken place, so that the blade of a scalpel could easily be thrust through from the outside into the iliac fossa.

In the two thigh bones, and in the clavicle, fracture had taken place. Subsequently a considerable amount of callus had been thrown out, and a certain amount of bony union had occurred. The fracture of the clavicle had taken place at the junction of the acromial with the sternal portion. The callus uniting the two ends was situated almost entirely behind and above the line of fracture, while anteriorly, where the cancellous tissue was extensively infiltrated by the new growth, no callus was formed, and the fragments, though in opposition with one another, remained separate. Above and behind the fracture the callus formed a conical projection of bone one inch in length, which ran upward in the anterior border of the trapezius.

A fracture of the thigh bones had taken place on each side at the junction of the upper with the lower two-thirds of the

shaft. In the case of the right femur (Plate IV.) the lower fragment was displaced upwards and inwards, and was rotated inwards, while the lower end of the upper fragment was abducted, flexed, and rotated outwards. An irregular mass of callus situated chiefly on the anterior aspect united the two fractured ends. The appearances in the left femur were practically identical.

The cancellous tissue at both ends of the bone was extensively infiltrated, and in some parts entirely destroyed by the new growth, which came to the surface through the thin shell of compact tissue at various places. The chief of these were (*a*) at a spot close to the attachment of the ligamentum teres to the fovea capitis, where the cartilage of the head had been destroyed by osteo-arthritis; (*b*) several places around the base of the great trochanter, and the lower and outer part of the neck; and (*c*) on the popliteal surface above the internal and external condyles. It is noteworthy that all of these, with the exception of the first mentioned, are situations in which large vessels enter and leave the bone. The encrusting cartilage of the head and condyles was, as is usual in malignant disease of bones, unaffected by the new growth, and it was only where destroyed by osteo-arthritis that the surface of the head of the femur was involved.

The lymphatic glands in Scarpa's triangle and in the inguinal region were involved on both sides of the body, and were imbedded in a mass of dense fibrous tissue, which also surrounded the femoral vessels. A similar condition was found in connection with the deep lymphatic glands of the neck, especially on the right side, where the carotid vessels and large nerves were firmly imbedded in a dense fibrous growth, which extended upwards into the parotid and submaxillary regions.

Although it was not till a considerable time after death that the condition of the bones was discovered, and I was able to obtain portions of the secondary growth for microscopic examination, the tissues were sufficiently well preserved for the histological characters to be recognized. Sections of the tumour taken from a block removed from the region of the parietal bone, and including a segment of the middle meningeal artery, shewed the following appearances in passing from within outwards.

The dura mater was thickened and infiltrated with a large number of small spheroidal, oval, and flattened "lens-shaped" cells, which were situated in the intervals between the layers of fibrous tissue composing the membrane. In this way several strata were formed which lay in planes parallel to the surface. The cells themselves were packed closely together without any intervening tissue. They had large rounded nuclei, and were epithelioid in appearance. A large branch given off from the middle meningeal artery could be traced for a short distance into the substance of the growth.

Immediately external to the dura mater was a layer composed of a fibrous stroma enclosing branched tubular spaces filled with cells. These spaces communicated freely with one another, and ran for the most part in a direction vertical to the surface, and thus at right angles to the plane of the dura mater. They varied considerably in size in different parts, and the amount of fibrous stroma separating them varied no less. In some places it formed a fine inter-alveolar reticulum, in others a dense cicatricial tissue, greatly in excess of the "cancer cells" contained within the spaces, the proportion of the areas occupied by the stroma and the "cancer cells" being about four to one. The epithelial cells occupying the spaces were small, granular, and irregular in form, and their nuclei were large in comparison with the amount of the surrounding protoplasm.

In the centre of the growth (the region of the former diploic tissue) the spaces were generally much larger and more alveolar in character, the tubular form and vertical arrangement being entirely lost. This part was also more vascular, and the cancer cells larger, more numerous, and less granular. Here and there a few of these larger spaces, containing masses or columns of closely-packed epithelial cells, were continued into the zone characterized by the tubular spaces just described; while some passed outwards into the region corresponding in position to the outer table, where the smaller type of alveoli was again predominant. The alveoli of this outer zone, however, did not exhibit the definite arrangement of tubules passing in a direction vertical to the surface which was met with in the region of the inner table. The pericranium, like the dura mater, was slightly thickened, and was infiltrated by epithelioid cells.

A careful study of this and other cases of secondary deposit of cancer in bone appears to be of importance when regarded either from a strictly pathological or from a clinical standpoint. With regard to the former, these cases indicate very clearly the route by which dissemination of the "cancer cells" is accomplished after these have entered the general circulation. They travel by the arteries which supply the different bones or viscera. In a large proportion of the reported cases of metastasis in which the vault of the skull has been involved, the secondary deposits are distinctly stated to have occurred symmetrically and to have followed the branches of the middle meningeal artery.

The exact distribution of the branches of this artery in the bone and membranes covering it has, so far as I am aware, not yet been fully worked out. I therefore injected the artery on one side of the head, in two specimens in which the vault of the skull was removed, without detaching the dura mater or the pericranium. In one specimen I employed Beale's "Carmine glycerin mass," and in the other Beale's "Acid Prussian blue glycerin mass." The colouring matter was seen on injecting the specimens to appear first as a number of minute specks on the internal surface of the dura mater in the lines of the main artery and its branches; it crossed over to the opposite side, extending beyond the sagittal suture for about $1\frac{1}{4}$ inches. The dura mater lining the frontal and occipital bones adjacent to the parietal was also injected. The fluid, moreover, passed freely into the superior longitudinal and parasinoidal sinuses, and escaped by the cut cerebral veins. The vessels of the pericranium, in positions corresponding to branches of the artery on the inside, were also injected, as was the case in the specimen of secondary deposit of cancer just described. In this latter specimen even the comparatively coarse injection used in preparing the body for the dissecting room (consisting of starch and a small quantity of cochineal dissolved in water) had apparently entered these vessels from the meningeal artery, as in the specimens employed for the experiment, and had not come from the temporal arteries. With regard to the arteries themselves in the cancer case, they were markedly tortuous, and could be seen both on the parts which were the site of the deposits and in the unaffected parts between and around them.

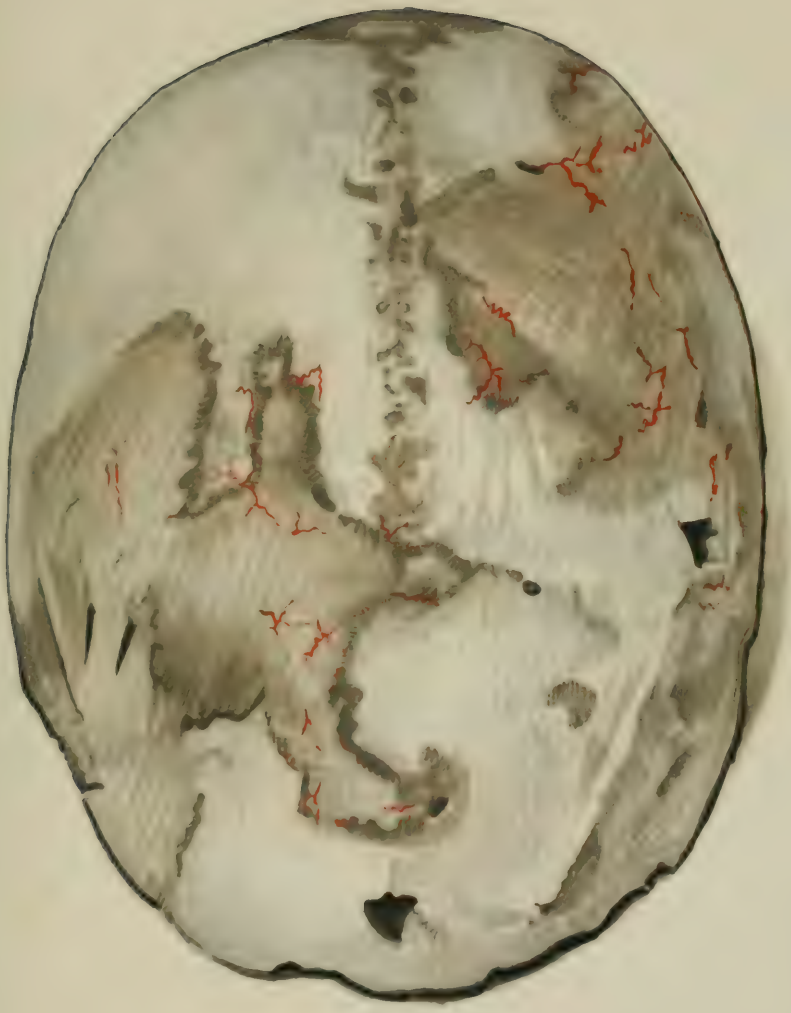
They were largest and most numerous in positions corresponding to the branches of the main artery on the inside; and we may conclude therefore that they were the original arteries of the part, or if not actual branches of the middle meningeal artery, that they were at any rate in very free communication with that vessel.

Microscopic examination of sections cut from decalcified "blocks," which were taken from the skull that had been injected with the Prussian blue solution, shewed that the fluid had lodged in large irregular spaces in the diploic tissue, which appeared to be the diploic veins. It would seem, therefore, that there is a free communication between the arterioles and venules without the intervention of small capillaries, capable of arresting the passage of the thick glycerine solutions employed in both specimens.

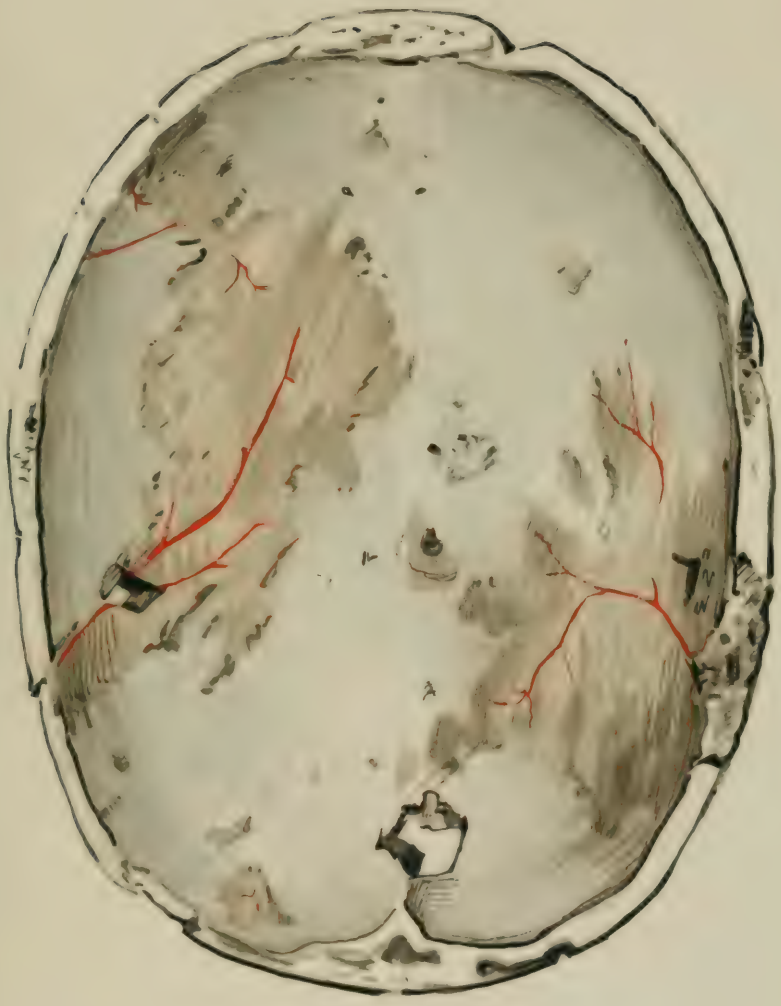
This free communication of the arteries of the bone with large irregular venous spaces probably favours the lodgment and growth of secondary carcinomatous deposits, for it is in situations where the bone is especially vascular, and the veins large, *e.g.*, in the bodies of the vertebræ, that these deposits are most common.

Other conditions, however, must be present which favour metastasis in bone, as in a large proportion of those cases in which cancer has become disseminated in other parts the bones escape. In the case which is the basis of this Paper osteo-arthritis was present, and the osteophytic outgrowths caused by this disease were specially affected by the new growth. It is possible that the disease had lowered the vitality of the bone at these points to such an extent that the tissues were unable to resist the growth of the "cancer cells." It is extremely probable that, in the same way as the occurrence of the primary growth appears to be favoured by a general lowering in vitality of the tissues such as occurs with the incidence of old age, or a local lowering such as occurs in consequence of previous inflammation with the formation of cicatricial tissue, so also the occurrence of secondary deposits, in one group of organs or in another, may be determined by the existence of some modification, whether recognizable or as yet unrecognizable, which has lowered the vitality of the parts and rendered them specially liable to be implicated by the invading cells.

Thus, assuming that the cancer cells in cases of general dissemination are carried by vessels passing from the original site of the cancer to all parts of the body, it appears that the selection of certain situations for the development of the growths will be determined not only by certain local conditions depending upon the *state of the circulation* in the particular part, or parts, but also by the *power of resistance of the tissues* to the growth of the invading cells.



Outer surface of the vault of the skull.



Inner aspect of the vault of the skull.

Upper part of the right femur, seen from behind.

SOME NOTEWORTHY CASES FROM THE CANCER WARDS, 1900—1903.

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The following is a brief account of some of the more interesting cases, from a pathological point of view, which have been met with among the patients who have died in the Special Cancer Wards of this Hospital.

(I.) *Remarkable Cases of Primary Malignant Disease.*

A girl, aged 19, was first admitted to one of the Surgical Wards with pyloric obstruction and successfully treated by gastrojejunostomy. The success, however, was short-lived, for in a few months' time she died in one of the Cancer Wards to which she had been transferred. The principal appearances seen on autopsy were: Considerable emaciation of the body. In the stomach, at the pyloric end, the walls all round were enormously thickened by a mass of colloid degenerated growth which entirely encircled the lumen, but was not ulcerated. The lumen was quite patent. Near the greater curvature a portion of the jejunum was adherent to the stomach (the result of gastrojejunostomy). The opening made into the stomach was about half an inch in diameter and quite clean, but close to it was a suture with the free end in the stomach, and also a small nodule—a secondary growth, in the stomach wall.

The appearance of the lungs when cut into closely resembled that of acute miliary tuberculosis. Along the course of the bronchi throughout the lungs were small grey nodules which, as a rule, in size and colour, simulated grey tubercles; in a few places where the nodules were larger (3—5 mm. in diameter) they obviously consisted of grey jelly-like masses. Other

secondary growths were met with in the posterior-mediastinal and lumbar lymph-glands, in the peritoneum, and in the right ovary; some of these metastases presented the same gelatinous appearance.

Microscopically the growth was found to be a spheroidal-celled carcinoma, but the great majority of the cells and the stroma were degenerated into shreds, and these stained very deeply with logwood. The "colloid" degeneration was well seen in the miliary deposits in the lungs. Whether this material was "colloid" in the sense of the term used by Ernst cannot now be ascertained.

The remarkable points in this case are: the early age at which the growth occurred (19), the large size to which the primary growth attained, the absence of any ulceration, the miliary deposits throughout the lung, and the "colloid" degeneration of the growths, even when of microscopic size.

Among males there have been in the Hospital, during this four-year period, four cases of primary carcinoma of the breast. They were respectively aged 50, 53, 64, and 86 years, and the last mentioned died in the Cancer Wards. Besides being remarkable for the age of the patient, this was a notable case for other reasons. For the man's lower lip was much shortened, and there was a special note to the effect that the patient affirmed this condition to be due to the removal of a cancer from it twenty years previously at the London Hospital.* If this be true, it would seem that we have here a case of two distinct primary malignant growths in the same person.

Besides this, at least two other patients have given a history of two primary malignant new growths.

One was a woman of 52, who died with carcinoma of the cervix of the uterus, which had invaded the body of the organ and extended into the pelvis. Her left breast had been amputated about six years previously for "scirrhus."

The uterine growth was a squamous-celled carcinoma.

* The following details have been kindly furnished by Mr. Hugh Lett, Surgical Registrar to the London Hospital. J. W. was admitted to the London Hospital on January 12th, 1880, with epithelioma of the lower lip, of five months' duration. The ulcer was situated in the middle line, in size equal to a shilling. Dresser says "very little induration, no enlargement of glands." The ulcer was excised by Mr. Adams. No mention of microscopical examination.

The other case was also that of a woman whose left breast had been amputated about six years before for cancer. She died in the Hospital in 1901 with a growth which had destroyed the cervix and lower part of the corpus, invaded the bladder, and had caused also a large recto-vaginal fistula. Secondary growths were found in the inguinal and aortic lymph-glands, the liver, lungs, left adrenal body, head of left femur, and second lumbar vertebra.

Microscopically they resembled the uterine growth—squamous-celled carcinoma; no cell-nests.

Yet a fourth case, and one very similar to the two last, seems to have occurred. The patient is still (April, 1904) alive, but cancer of the cervix uteri has been diagnosed clinically. The patient was in this Hospital for cancer of the left breast about eight years ago. The breast was amputated, and since then several recurrences have been removed. Microscopically the mammary growth is an atrophic spheroidal-celled carcinoma. This case is mentioned by Foulerton as one of those treated with extract of thymus and thyroid gland in the Reports from these Laboratories, Vol. II., pp. 144[6], 144[7].

A very interesting case, on account of the microscopical appearances from different parts, and because the patient had been treated by the "X-rays," was that of a woman who died at the age of 64 from bronchitis in February, 1902.

Mr. Andrew Clark, who had charge of the case, published an account of her in the "British Medical Journal," 8th June, 1901, as one in which the "X-rays" had proved beneficial.

The growth was one of the right breast, which was first noticed in 1890; it had increased slowly in size until in 1898, when it was about two inches in diameter, the skin over it commenced to ulcerate. "X-ray" treatment was employed for ten months with apparent success, from March 6th, 1901, until January 10th, 1902.

At the post-mortem examination the site of the right breast was occupied by an ulcer reaching from the mid-line for a distance of about eight inches to the axilla; vertically it measured about six inches. Its floor was smooth and the margins shelving, but close to the lower edge was a quite small, but hard, nodule in the subcutaneous tissue, and at the outer margin nearest the axilla was a globular mass about an inch in

diameter, which was intensely hard under the knife and presented a very white appearance on section.

On the left side, at about the middle of the inner wall of the axilla, was a rounded mass of rather soft growth, about half or three-quarters of an inch in diameter.

Microscopically the ulcerated part of the breast and the mass from the right axilla shewed very marked fibrosis. This was especially the case with the axillary mass, which practically consisted of nothing but fibrous tissue, a very few small and irregular spaces and crevices being present, and these containing apparently only the degenerated remains of cells of the new growth.

The nodule from the breast and that from in front of the sternum shewed a thick layer of fibrosis, and below this, carcinoma with a large proportion of fibrous tissue.

The lymph-gland from the left axilla differed from the other growths which had been subjected to the "X-rays" to as great an extent microscopically as it appeared to do macroscopically. It shewed a spheroidal-celled carcinoma of a type very similar to the others, but with very little connective tissue, while the cells were larger and had larger bodies in proportion to their nuclei.

It was obvious that the epithelial cells of the secondarily affected lymph-gland were actively growing in contradistinction to those from the parts which had been under "X-ray" treatment, though no idea could be formed as to the rate of growth. It is not a little remarkable that in a woman whose primary growth was characterized by atrophic conditions far exceeding those met with even in atrophic scirrhus, as we usually see it, one of the secondary growths should be so flourishing, and characterized by possessing very little connective tissue.

This case may be taken as a good example of an atrophic growth. The case of the woman mentioned above, who was treated by extract of thymus and thyroid glands, is of a similar nature, and many others have occurred also, but hardly to the same extent. The most remarkable one, however, in this respect was that of a man who died in the Cancer Wards at the age of 79 from bronchitis. He had been admitted for carcinoma of the rectum, but the growth gradually became quiescent, so that at the autopsy the large cancerous ulcer had quite a smooth

floor; it measured about four inches in vertical extent, and the lumen of the bowel was not narrowed. No secondary growths. Microscopically it proved to be columnar-celled carcinoma. In contrast to these atrophic cases in old people may be put the case first mentioned in this Paper of the girl, aged 19, with the large pyloric growth.

Not only the size of the neoplasm but the rate of its growth increase with the earlier onset.

These occurrences are of course well known, but the cases are mentioned here as good illustrative examples. The fact, too, that such variations according to age of onset are met with is probably of considerable moment in the etiology of carcinoma.

The duration of the disease in the case aged 19 was eighteen months, in the woman treated by "X-rays" about 5½ years, in the rectal case about three years.

Early onset, accompanied by rapid and extensive growth, was also well seen in a case of sarcoma of the frontal bone in a woman of 32. The growth attained a large size, and projected some 4½ inches. The whole duration of the case was eleven months, and during this time one large mass was removed, but recurrence took place, and the growth attained to the same size again. In this case there was a history of a blow on the forehead.

A few of the cases of primary carcinoma have been of interest more on account of their unusual situation than for any peculiarities of the growth itself. One of these was a primary carcinoma of the right external auditory meatus in a man aged 45. The growth was of the squamous-celled type.

Another growth began in the duodenum, an inch below the bile papilla, and invaded the pancreas. The growth was a columnar-celled carcinoma. The patient was a man aged 49; he had secondary growths in his liver and in the neighbouring lymph-glands.

A third case has an interest beside that of unusual position. Microscopically it is regarded as an endothelioma. The patient, a woman of 29, had undergone several operations for disease of the middle ear.

At the post-mortem examination the right pinna was found to be small, and the external auditory meatus small and blocked up for more than its inner half. Above and behind the meatus

was the deep pit of a "mastoid operation." Above the ear was a slight bulging, largely due to thickening of the epicranium, but also largely due to growth. The right temporal bone was replaced over a large area by a moderately firm, partly fibrous growth, the base of the petrosal portion and the adjacent part of the squamosal being principally affected. Externally the growth was limited by pericranium or the outer table of the skull. Internally the growth formed a half-hemispherical mass, of which one of the flat sides was applied to the inner surface of the squamosal, and the other to the surface of the petrosal in the middle cranial fossa and the upper surface of the tentorium cerebelli. Below the tentorium, however, a mass was also seen composed of numerous small bosses, projecting backwards and inwards into the anterior and external part of the posterior fossa. The tentorium itself appeared to be unaffected. No dura mater could be found covering the growth. The size of the tumour was about 6 cm. from before backwards, 8 cm. from above downwards, and 4 or 5 cm. from within outwards. When cut across it was found to consist of a somewhat firm and fibrous slightly vascular tissue. The growth pressed on the brain without invading it.

(II.) *Remarkable Cases of Secondary Malignant Disease.*

In several cases the secondary deposits of new growth have presented points of interest regarding either their distribution or secondary changes.

(*a*) The most remarkable in the way of distribution was the case of a woman of 58, who had had her right breast removed for carcinoma.

She suffered from spontaneous fracture of both femora, which were the seat of large masses of new growth at about the junction of the upper and middle third.

At the post-mortem examination the other secondary growths were found in the middle line of the frontal bone, in the lumbar vertebræ, and in the mesenteric glands. The symmetrical distribution of the growths and their occurrence only in bones, with the exception of those in the mesenteric lymph-glands, make this case remarkable; in particular, there were no nodules

in the skin. Microscopically the growth was a spheroidal-celled carcinoma.

(*b*) The occurrence of secondary new growth in the left supraclavicular lymph-glands is interesting in cases of carcinoma in the abdomen, as indicating the transference of carcinoma along the thoracic duct.

Seven cases of this nature have been met with, while a similar condition occurred also in a case of sarcoma, which commenced in the left ischio-rectal fossa. The patient was a woman of 26, and at the time of her death was extremely wasted. The lumbar lymph-glands were also the seat of new growth.

Of the seven carcinoma cases one was a male, aged 59, who had columnar-celled carcinoma of the pylorus, one was a female of the same age suffering from a like condition, and the remaining five cases were squamous-celled carcinoma of the uterine cervix.

A list of the cases is given, together with some of the principal features at the autopsy. A striking point in connection with this condition is the general absence of symptoms, and especially of that of dropsy, which might *a priori* be expected. This appears, however, only to hold good if the lymphatic glands and channels (excluding the cœliac glands) alone are concerned. Thus four cases in which the pelvic or lumbar lymph-glands only were infected shew neither ascites nor excess of pleural or pericardial fluid, nor yet any cutaneous œdema; whereas if the liver or cœliac glands are infected, then œdema or collection of fluid in serous cavities is noted. In the latter case the difference is probably the result of pressure on the inferior vena cava. Two instances, however, were met with where the thoracic duct was actually blocked, and chylous ascites occurred. There is no marked evidence that duration of disease, sex, or age have any influence on the occurrence of this infection of the supraclavicular lymph-glands.

In one cervix case the right supraclavicular gland was the seat of secondary deposit, and in one stomach case both right and left supraclavicular glands were infected.

In two other cervix cases the left supraclavicular lymph-glands were enlarged, but no infection by new growth was found microscopically.

A most remarkable case occurred among the autopsies on

cases other than those dying in the Special Cancer Wards. It was that of a man, aged 61, where the thoracic duct itself was the seat of new growth for a considerable part of its extent, and so too were the lymphatic channels leading from the primary growth, which was in the sigmoid flexure, to the lumbar lymph-glands and thence to the thoracic duct. In this case there were no symptoms pointing to his condition, and that seems to have been the verdict of many of those who have recorded similar cases. The case is recorded in "Trans. Path. Soc. Lond.," vol. liv., p. 153, and does not really belong to this series of cases, but is mentioned in this connection as being an extreme case.

(*c*) Regarding now the cases in which remarkable degeneration or other changes in secondary new growths have occurred, mention may be made of instances in which it is probable that the psoas muscle was invaded by a growth that subsequently broke down and became cystic.

All the bodies in which this condition was found were cases of primary carcinoma of the uterine cervix. They are here given in order of age.

(1) Female, aged 35, squamous-celled carcinoma of the cervix of the uterus extending to the vagina and left broad ligament and ovary.

The pelvic and lumbar lymph-glands were infiltrated extensively by new growth. Underneath the right psoas muscle, a cavity formed by broken-down growth extended from the pelvis up to about the second lumbar vertebra. The fascia covering the psoas had been destroyed. A smaller cavity perforating the obturator fascia was present on the left side.

(2) Female, aged 45, squamous-celled carcinoma of the uterus, which had been removed. Secondary growth in lumbar lymph-glands. On the right side of the body was an enormous cyst. It extended from the under surface of the liver above, on a level with the first lumbar vertebra, downwards under Poupart's ligament to half-way down the thigh—some four inches below the lesser trochanter. The boundary on its left side was the vertebral column for the upper part, but in the pelvis the cyst extended to nearly half-way across the left iliac fossa. In the thigh, the linea aspera could be felt near the inner boundary of the cyst. To the right it extended in the

abdomen outwards nearly as far as the mid-axillary line, and then its wall came forward with the cæcum and ascending colon lying in front of it. The contents of the cyst measured more than seventeen pints. The fluid which first escaped was clear brown and of oily consistence. As the cyst was emptied the fluid became thicker and whiter; later on several flakes, and finally pieces of soft white growth appeared. These last came from a soft growth which apparently had eroded the sacrum and inner surface of the ilium and ischium of the right side. The smooth head of the femur was visible from within the pelvis and projected slightly through a hole, which had a rough eroded margin.

Both ureters passed free through the cyst to the bladder. The external iliac vessels also passed through it unaffected. On the posterior wall were seen the nerves of the lumbar plexus. No psoas muscle was seen, and the right sides of the bodies of the vertebræ were bare. The iliacus and its attachment to the lesser trochanter remained.

(3) Female, aged 47. The primary growth was a squamous-celled carcinoma, and there was no obvious secondary infection of the lymph-glands.

The right psoas muscle above the brim of the pelvis was seen to be enlarged, and fluctuation was obtained in it. The swelling consisted of a thick-walled cyst containing clear reddish fluid. The wall of the cyst appeared to consist of secondary growth; it included in its substance the external and internal iliac vessels. The external iliac artery was entirely blocked.

The wall of the cyst, microscopically, was found to be composed of growth similar to the primary lesion.

(4) Female, aged 49, squamous-celled carcinoma of the cervix of the uterus, extending forwards to the bladder and laterally to each fornix. The inguinal glands on each side and some of the iliac and lumbar glands were infected and had become softened and broken down.

Situated on the left psoas muscle, apparently within its sheath, was a thin-walled cyst containing a turbid fluid. The fibrous wall of the cyst appeared, microscopically, to have epithelial cells lining it.

Two other cases suggest a possible explanation of the occurrence of these cysts.

One was that of a woman, aged 34, who died of malignant disease of the anterior wall of the vagina. Microscopically, squamous-celled carcinoma.

The lymph-glands on each side of the pelvis along the iliac vessels were infected, chiefly those on the left side, which had pushed aside the psoas muscle outwards from the brim of the pelvis. There were no other secondary growths.

The other case was one of squamous-celled carcinoma of the uterine cervix in a woman of 59.

At the brim of the pelvis on the left side was a rounded mass of soft white new growth, about two and a half inches in diameter, which pushed outwards the psoas muscle.

Other secondary growths found in this case were in the rectum, the pelvic and lumbar lymph-glands, and a left supra-clavicular gland.

It appears at least possible that the growth from such glands might eventually have extended into the psoas, whose sheath would have been thinned by stretching, and that then with its rapid extension the growth, centrally, would degenerate and undergo liquefaction.

(*d*) Of other cases remarkable for changes in the secondary growths may be mentioned one of a woman, aged 45, with primary spheroidal-celled carcinoma of the breast. Her body at the time of death was covered with nodules of varying sizes up to about an inch in diameter, and the great majority of these were ulcerated, a condition which must be considered as very uncommon. Her case is referred to by Foulerton in Vol. II. of the "Reports from the Cancer Research Laboratories," page 144[5], as having been treated by thymus serum, and it is there suggested that the extensive ulceration might be, in part, ascribed to the action of the serum.

Table of Cases shewing conveyance of Malignant Cells along the Thoracic Duct.

Sex.	Age.	Primary growth.		Duration.	Secondary growths.	Thoracic Duct.	Supra-clavicular glands.	Wasting.	Œdema of lower extremities.	Fluid in cavities.		
		Site.	Nature							Pericardium.	Pleura.	Peritoneum.
F	26	Ischio-rectal fossa.	Sarcoma.	.. ..	Lumbar lymph-glands.	.. ..	Left.	+	..	.. ..	..	.. ..
F	30	Cervix of uterus.	Carcinoma, squamous-celled.	19 months.	Pelvic and lumbar lymph-glands.	.. ..	Left.	+	..	.. ..	..	.. ..
F	37	Cervix of uterus.	Carcinoma, squamous-celled.	19 months	Pelvic and inguinal lymph-glands, lung, ovary, peritoneum.	Occluded by pressure of supra-clavicular glands.	Left.	0	..	4 ozs. turbid.	Right, 50 ozs.; left, 65 ozs.	Chylous ascites.
F	38	Cervix of uterus.	Carcinoma, squamous-celled.	11 months.	None.	.. ..	Left.	+	..	.. ..	..	.. ..
F	43	Cervix of uterus.	Carcinoma.	14 months	Lumbar lymph-glands and liver.	.. ..	Right.	+	+	.. ..	..	.. ..
F	59	Cervix of uterus.	Carcinoma, squamous-celled.	21 months.	Pelvic and lumbar lymph-glands.	.. ..	Left.	+	..	.. ..	..	.. ..
F	59	Pyloric end of stomach.	Carcinoma, columnar-celled.	4 months.	Lumbar and coeliac lymph-glands; stomach wall.	.. ..	Right and left, caseous, partly liquefied contents.	+	+	.. ..	Right, 14 ozs.; left, 19 ozs.	.. ..
M	59	Pyloric end of stomach.	Carcinoma, columnar-celled.	10 months.	Lumbar and coeliac lymph-glands, liver, kidneys, right adrenal.	Plugged.	Left.	+	+	.. ..	Left, 12 ozs.	.. ..

STATISTICS OF CARCINOMA BASED ON THE RECORDS OF THE MIDDLESEX AND THE ST. GEORGE'S HOSPITALS.

(Plates V.—VIII.)

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Among the many pressing questions which are occupying the attention of all those who are engaged in research upon the subject of cancer, one of the most important is that of determining whether or not at the present time there is an increase in the incidence of the disease. It is not necessary here to point out the arguments that have been used when supporting one side or the other of the controversy, for short of an actual investigation it is impossible to arrive at any decision, and even when one has collected a considerable mass of data it is by no means easy to ascribe to them a correct value.

It is clear that if a thousand infants had been taken at random in the year 1800, for example, and the causes of their deaths had been registered with the greatest care, that we should have had a certain amount of evidence as to the incidence of cancer in that population of 1,000 souls. Figures so obtained could have been compared with similar figures derived from a population of 1,000 born in the year 1810, and so on. With such data one could have arrived at some sort of an idea as to whether cancer was on the increase or not. Such statistics, however, are of course entirely wanting; nevertheless one can in some measure form a population from the records of a hospital.

It is clear that if a person dies in a hospital at the age of, say, 50 years, the actual year of his birth can be deduced from

the year of his death. The point is an extremely simple one; but since upon it the entirety of the following Paper is based, it will be well to put forward the matter quite clearly. If we take the post-mortem records of a hospital over a number of years and mark each case on a previously prepared sheet under the year of his birth, we shall in course of time become possessed of a "population" born in each year, of each member of which we shall know the cause of death. It is true that the populations will be small ones, and that at the beginning and the end of the series we shall certainly not have a sufficiency of cases upon which to speak; but in the middle of the series a fair number of cases will accumulate.

I.—METHOD OF OBTAINING STATISTICS.

The actual method employed in accumulating the statistics here presented was not absolutely that indicated in the preceding paragraph. Two things were clear. The first was that if we took all deaths at all ages the figures would become unmanageable. The second objection was a far more serious one. Before about 1880 the distinction between carcinoma and sarcoma was not made, and the safest way to avoid inclusion of cases of sarcoma amongst the carcinomatous cases that were the sole subject of investigation was to choose an age which was high enough to exclude the great majority of sarcomatous cases, while it was low enough to include the great majority of cases of carcinoma. Hence the age 35 was taken, and all persons dying at the age of 35 or upwards were included in our lists. The same age also serves to eliminate variations due to improved hygiene, etc., in the case of "preventible" diseases, since these usually affect persons below the age of 35 years.

These preliminaries having been settled, large sheets were prepared with sub-divisions corresponding to the years of the nineteenth century. Then, taking the post-mortem books and the clinical records for each year in succession, each case aged 35 years or upwards was entered under the year in which he was 35 years of age. In this way we succeeded in obtaining over a period of about eighty years a population for each year, of each member of which we knew the cause of death. Further, it is clear that we were justified in the large majority of cases

in concluding that at that age of 35 the individuals were healthy, for the great number of them did not die till ten, twenty, or thirty or more years after.

In this manner the records of the two hospitals were dealt with. Males and females were kept separately and deaths were noted as being due to carcinoma or non-carcinomatous. Hence on conclusion of the accumulation of data we were in possession of the facts that—

> x persons who were 35 years of age and healthy in year A died of cancer, while y persons died of non-cancerous diseases.
>
> x' persons who were 35 years of age and healthy in year B died of cancer, while y' persons died of non-cancerous diseases,

and so on. By comparing the figures thus obtained it was hoped that an indication of the incidence of cancer during a considerable number of years might be obtained, and that this might be not only of interest in reference to the past, but also of use in indicating the course that the disease is likely to take in the immediate future.

In accumulating the statistics it has already been mentioned above that the clinical records were used as well as the post-mortem records. This was done for two reasons. Firstly, the clinical records extend over a longer period of years than the post-mortem notes,* and secondly, a very fair proportion of the patients do not actually die within the walls of the hospital, but go home to die. Bearing these two facts in mind, it was evident that a selection of cases had to be made. In the case of those who died in hospital and were subjected to post-mortem examination it was usually enough to read through the written description of the macroscopic appearances to come to a fairly accurate conclusion as to whether the disease was or was not carcinoma. Even at a very early date the diagnoses as to carcinoma or non-carcinoma need but little revision, although in some cases it appeared that the condition might have been one of those which at the present time we know to be dependent upon streptothricial infection. Cases such as these were invariably ignored. But there can be little doubt that in the vast

* This is not the case at St. George's Hospital, where the post-mortem records extend back twenty years earlier than the clinical notes.

majority of cases post-mortem diagnoses of cancer of the stomach or of the breast, uterus, lip, tongue, intestine, œsophagus, were quite accurate, especially as the post-mortem record also gives information of any metastases.

In dealing with the clinical records more care was necessary. For that reason all diagnosis of "cancer of the stomach" in a person who did not die and undergo post-mortem examination was rejected entirely. So, too, the term "abdominal tumour" was regarded as of insufficient accuracy or definiteness to warrant an inclusion under either the cancerous or the non-cancerous group, and therefore all cases bearing this diagnosis were ignored. On the other hand, when a man aged 60 years or upwards was said to be suffering from cancer of the œsophagus or stricture of the œsophagus, and was said to have left the hospital "unrelieved" or *in statu quo*, it was taken that the diagnosis was probably one of carcinoma, and unless some detail in the clinical notes distinctly suggested that the condition was traumatic or the result of corrosive poisoning, the case was included amongst the cancerous group.

In respect of the non-cancerous group the following cases in which the patient did not die in the hospital or was not the subject of an autopsy were reckoned:—

(*a*) All persons above the age of 35 suffering from thoracic or abdominal aneurysm.

(*b*) All persons above the age of 60 the subjects of either heart disease, renal disease, or hemiplegia, or stricture of the urethra, or enlarged prostate.

(*c*) All persons above the age of 65 the subjects of fracture of the thigh.

(*d*) All persons above the age of 70 suffering from chronic bronchitis and emphysema.

In the cases in which one of the foregoing diagnoses was made, the chance that the existence of cancer was overlooked or that the patient would ultimately have died of cancer is so small as, practically, to be negligible. In the third class, it is true, there is a certain amount of danger that the fracture may have been the result of a local metastasis of new growth in the bone, but the difference in the history is usually sufficient to distinguish between a traumatic fracture of the femur in an old person from a spontaneous fracture the result of a bony metastasis.

II.—CRITICISM OF METHOD: SOURCES OF FALLACY.

In some measure these points have been considered in the first section, but a few remarks further are necessary.

(*a*) From the very nature of the case it is clear that the results deducible from the statistics given below cannot be directly applied to the entire population. For not only is the class from which a hospital draws its patients insufficiently representative of the entire community, but also, as the statistics themselves shew, there is a marked difference between two hospitals in regard to their experience of cancer; and that, too, in spite of the fact that they may be situated no more than a couple of miles from one another in the same city, and are of practically the same size. What the statistics undoubtedly shew is only the experience of the particular hospital. Nevertheless the fact that there obtain such differences between the incidence of cancer at The Middlesex Hospital and at St. George's serves to intensify the importance of any cases in which their individual experiences agree.

(*b*) It is a question how far we are justified in considering that the populations we have formed by the methods that have been described can be considered as "healthy." After all, this difficulty obtains equally in the case of a population taken at birth, for it is certain that a considerable proportion of those lives which terminate within the first year after birth were not healthy from the first. It may be said that a person dying in our specially prepared populations at the age of 35 or 36 had already the commencement of cancer within him, and therefore could not be considered as a healthy life at the age at which he was included in our lists. But it is clear that an infant dying during the first or second year of congenital syphilis was equally not healthy at birth, and if the one method of calculating statistics is allowable there is no reason why the other should not be accepted. With every year beyond the initial one chosen that the person lives the presumption that he was healthy at the initial age increases, or to be more accurate, the presumption increases that he was not at the initial age the subject of cancer. Naturally this contention tacitly implies a disbelief in the view that cancer is a congenital disease in the sense that a person who suffers from it was endowed with the rudiments of it at

birth, and that these rudiments increase in potency as his age increases. And lastly, although it must be conceded that our lack of power to recognize cancer does not necessarily imply that cancer is absent, yet it would be thoroughly unscientific to assume its presence when we fail to recognize it at all, and especially when we believe, from all our accumulated experience of the disease, that its manifestation in one way or another is not delayed many months after it comes into, at all events, the earliest possible recognizable existence.

(*c*) To a certain extent error has crept in during the earlier years of the series owing to faults in the records. Thus for some unexplained reason we have been unable to find the records of The Middlesex Hospital for the years 1847—52. This does not invalidate our figures, for the only result is that we have a smaller series of cases wherewith to form our populations for the years about 1820. As we do not claim that the figures are sufficient for drawing any comparisons before about 1830, the lacuna, though regrettable, is not fundamental. A more serious fault is that in some of the earlier years of the series there has obviously been a remarkable laxity on the part of the Registrars. Thus during the years from 1862—66 we only find recorded altogether 41 cases of carcinoma in women, although the number of cases occurring in men is about the average. Here the difficulty is not in the matter of forming the populations, but in deciding whether the lacuna affects cancerous women only or obtains also in the case of the non-cancerous, and in trying to form an estimate as to the ratios borne by the cancerous admissions to the total admissions into the hospital.

(*d*) Concerning errors in diagnosis something has already been said. It is certain that a failure to distinguish between carcinoma and sarcoma on the part of the older surgeons is the most fruitful source of fallacy in our figures. It has already been indicated that we have endeavoured to guard against this fallacy as much as possible by fixing our initial age at 35. Nevertheless it is equally certain that a small number of cases of sarcoma must have crept in, especially as our recent experience at The Middlesex Hospital, as the result of systematic microscopic examination of all the growths is that sarcoma is by no means so constantly a disease of young adult life and childhood

as is generally supposed. Figures given in the preceding reports from the Laboratories shew that a considerable proportion of cases is met with even in advanced middle age. Against this source of error it has been impossible to guard entirely, although we have had the point constantly in our mind when reading through the reports; and in all cases in which there has been a possibility from the description of the primary growth or from the distribution of the metastases that we were dealing with a case of sarcoma, that case has been omitted.

In the case of endotheliomata the matter is different. From our present standpoint we must feel sure that a certain number of cases of this type of growth has been incorporated. Judging from the relative infrequency with which they are met with at the present day, when we are fully alive to their existence, it does not appear probable that the error introduced by their inclusion is a large one. Nevertheless it is assuredly present, for it is quite impossible to distinguish cases of endothelioma of the breast, for example, from carcinoma of the organ—except microscopically. In the case of the brain, on the other hand, the probability that a so-called "cancer of the brain" was really either an endothelioma or a sarcoma is so great that all cases with this designation have been rejected. The same is true of primary disease of the pleura and the peritoneum, and these cases have also been rejected, or at least each has been carefully read through and treated on its merits.

(*e*) Age.—The age question has been a difficulty, and is a source of error in two ways. First, since the population of a hospital is drawn from the lower classes, there is a certain amount of unavoidable indefiniteness about the ages given. This is well shewn in the case of the men by the accumulation of cases at the ages multiples of five, and amongst the women by their accumulation at about the preceding integer. Apparently, the disinclination of women to overstate their ages shews itself even here. The statistics seem to shew that if a man and a woman are of the same age, but are uncertain what that age is, the man will give his age as, say, 50, while the woman will give it as 49. This difficulty obtains throughout the series, and accounts in a considerable measure for the irregularity of the curves. Moreover, there can be little doubt that ignorance as to age must have been a weightier factor in the earlier years of

the entire series, owing to the general lack of education of the lower classes.

In the second place, the age question presents sources of error, owing to the fact that amongst the patients forming our populations we have included numerous instances of persons who did not actually die in the hospital. In the case of such persons we have always taken the age given on admission. The period covered by their stay in hospital does not introduce any error of noticeable magnitude, but it is clear that we are entirely ignorant of the ages at which these patients actually died. All that can be said is that, from the nature of the cases, whether they were carcinomatous or non-carcinomatous, there is but little likelihood that they would have survived for a considerable number of years after leaving the hospital. This is more probably approximately true of the non-carcinomatous cases, as a glance at the list of the diseases accepted and the ages of admission will shew. In the case of carcinoma we are on more uncertain ground. In fact we are certain that the after-life of a patient who has undergone amputation of the breast under modern methods is considerably longer than it was when the operation was performed in a crude fashion, or when the dangers of pyæmia largely forbade operation altogether. For these sources of error it is impossible to allow, but since they are spread over the entire series, it is thought that they do not materially interfere with the general accuracy.

With the preceding remarks, which apply equally to The Middlesex Hospital statistics as to those obtained from St. George's Hospital, the way is cleared for a consideration of the data we have obtained. It will be well to consider each Hospital separately on identical lines, and afterwards to compare the two sets of results.

III.—STATISTICS OF CARCINOMA FROM THE MIDDLESEX HOSPITAL.

A.—*The Amount of Material.*

Although the records of The Middlesex Hospital date from 1746, yet the records of the years up to about 1843 are so scanty that they have been practically of little use in the present research. Further, though from self-evident causes, the value of the records

increases as one approaches towards the end of the nineteenth century, yet the case-books of the years of the middle of the century are satisfactory. In forming the "populations" it is clear that a record of a given year furnished data for a number of years previous, and often earlier by twenty or more years. These populations, however, were so small when they were derived from the earlier Registers that they were useless for combination into the Tables here presented, although they have been incorporated in the curve given on Plate VI. from the year in which cancerous and non-cancerous cases of both sexes were recorded. Thus, the first entry on the curve is one for the year 1814, but it is not until the year 1829 that we have become possessed of a population of 50, which is the minimum we consider reasonable to include in the statistics upon which argument can be based. The same paucity of cases obtains at the latter end of the century, but for a different reason, as will appear when the curve itself is under discussion.

In all, 13,061 cases have been analyzed. Of these, 6,507 were male cases, and 6,554 female. Of the 6,507 cases in men, 2,080 were cases of carcinoma, and 4,427 cases of other diseases than carcinoma. Of the 6,554 female cases, 4,126 were carcinomatous, 2,428 were non-carcinomatous. Table I. gives a full list of the several years, with the number of cases that were accumulated under each.

With reference to the actual number of cases that have been gone through in the records in order to obtain the data given in the following Table, there is no necessity to know them exactly. Probably they amount to about 130,000. From 1870 to 1900 they number over 83,000. The latter figure was accurately determined in order to arrive at the ratios borne by the cancer admissions to the total admissions to the Hospital during that period of thirty years, a point which is dealt with in the following section.

B.—*The Ratios borne by the Cancer Admissions to the General Admissions at The Middlesex Hospital.*

It is impossible to give the figures for the entire series of years, since in the earliest years we are not certain that all cases, cancerous and non-cancerous, were recorded. Table II. gives

TABLE I.

Cancerous and Non-Cancerous Age 35 Populations, Compiled from the Records of The Middlesex Hospital.

Year.	Males.		Females.		Year.	Males.		Females.	
	Cancer.	Non-Cancer.	Cancer.	Non-Cancer.		Cancer.	Non-Cancer.	Cancer.	Non-Cancer.
1801	0	1	0	0	1851	33	75	62	50
1802	0	0	0	0	1852	20	72	61	50
1803	0	0	0	1	1853	34	95	75	48
1804	0	0	0	0	1854	42	91	60	48
1805	0	0	0	2	1855	38	85	79	46
1806	0	1	1	1	1856	40	92	78	48
1807	0	0	0	0	1857	41	68	65	50
1808	0	1	0	3	1858	37	83	75	54
1809	0	2	1	1	1859	44	100	74	31
1810	0	2	1	1	1860	41	83	86	29
1811	0	0	0	4	1861	51	82	84	43
1812	1	2	0	2	1862	39	85	77	60
1813	0	6	1	1	1863	65	69	97	34
1814	1	3	2	1	1864	42	93	90	59
1815	4	6	1	7	1865	37	106	113	44
1816	2	5	1	5	1866	39	85	104	43
1817	1	4	1	5	1867	49	102	89	40
1818	3	10	1	4	1868	49	83	98	47
1819	4	6	3	6	1869	43	86	90	44
1820	2	11	4	9	1870	55	55	93	24
1821	1	10	3	2	1871	50	75	101	45
1822	2	10	3	9	1872	58	98	117	55
1823	4	7	4	7	1873	45	74	104	41
1824	7	10	9	10	1874	33	74	85	40
1825	8	13	5	9	1875	59	93	99	37
1826	3	15	8	12	1876	48	83	89	35
1827	4	30	12	12	1877	36	62	101	33
1828	8	24	7	10	1878	51	62	68	29
1829	9	17	9	20	1879	44	65	73	19
1830	2	27	14	15	1880	40	48	75	37
1831	4	20	9	13	1881	41	48	81	34
1832	12	30	14	16	1882	35	43	72	27
1833	15	39	10	15	1883	35	47	50	29
1834	9	36	18	36	1884	45	46	65	18
1835	20	48	24	33	1885	27	51	66	34
1836	9	45	12	34	1886	36	47	64	37
1837	12	38	17	21	1887	24	54	47	32
1838	15	47	38	19	1888	21	44	62	22
1839	13	49	23	26	1889	14	41	40	17
1840	11	54	39	26	1890	10	34	41	21
1841	18	51	38	28	1891	11	35	29	22
1842	16	55	34	38	1892	17	30	39	23
1843	14	53	41	36	1893	9	28	23	16
1844	22	61	50	30	1894	10	30	20	10
1845	23	90	59	39	1895	12	23	33	21
1846	26	70	41	22	1896	6	27	15	11
1847	24	77	46	38	1897	4	20	23	11
1848	23	79	59	36	1898	6	12	4	11
1849	26	81	63	45	1899	3	8	10	8
1850	32	80	50	46	1900	1	9	3	6

the actual figures, and on PLATE V. are curves in which the same points are shewn graphically for the thirty years from 1870 to 1899.

Over the same period the population of London (15 miles radius from Charing Cross) was as follows:—1871, 3,885,641; 1881, 4,766,661; 1891, 5,633,806; 1901, 6,581,372.

TABLE II.

Cancer and General Admissions to The Middlesex Hospital, 1870—99.

Year.	Female Cancer Admissions.	Male Cancer Admissions.	Total Admissions to Hospital (both sexes).	Percentage of Total Cancer Admissions to Total Admissions.
1870	73	25	1992	4·9
1871	75	15	1760	5·1
1872	93	25	1861	6·3
1873	77	44	2344	5·2
1874	94	34	2571	5·0
1875	99	32	2650	4·9
1876	92	20	2334	4·8
1877	68	29	2222	4·4
1878	98	38	2040	6·6
1879	84	39	2596	4·7
1880	92	39	2510	5·2
1881	93	46	2699	5·1
1882	98	50	2833	5·2
1883	86	32	2638	4·5
1884	103	48	2550	5·9
1885	94	61	2689	5·7
1886	109	43	2859	5·3
1887	102	48	2384	6·3
1888	101	54	2835	5·5
1889	104	45	2948	5·1
1890	108	54	3109	5·2
1891	119	61	3018	6·0
1892	103	60	2911	5·6
1893	90	49	2471	5·6
1894	114	64	3182	5·6
1895	117	60	3280	5·4
1896	125	75	3318	6·0
1897	131	59	3263	5·8
1898	113	63	2667	6·6
1899	141	96	3331	7·1

From these curves it is clear that if we omit all attention to individual years, there has been a remarkable parallelism between the increase in population, the increase in the number of general admissions to the Hospital, and the cancer admissions, even though the latter are considered under the two sex headings.

It is true that there has been a definite, although a very small, percentage increase in the cancer admissions as shewn by the slight upward tendency of the curve, formed of crosses, which represents the percentage borne by the cancer admissions to the general admissions, and this fact will call for consideration later. But on the whole it may be said that the greater the population of London, the greater the number of admissions to the Hospital, and the greater the number of admissions for cancer. How far it is justifiable to argue from the data of the thirty years 1870—99 that the same holds good over the entire series of years, covered by the statistics which form the basis of this Paper, is another matter. Considering the great uniformity of the curves over what is, after all, a fairly long period, it does not seem unjustifiable to conclude that the same parallelism has obtained throughout.

This parallelism is one of the greatest importance for our present purpose. Of itself it suggests that any actual increase in the number of cancer admissions is only dependent upon an increase in the population. But this supposition is not justifiable, for although the number of admissions to the Hospital has increased per annum, this has not occurred because the Hospital has enlarged *pari passu* with the increase in the population. As a matter of fact the increased number of admissions to all hospitals in recent years has depended upon a diminution in the length of stay within the hospital, rendered possible by the more rapid healing of wounds under antiseptic and aseptic treatment, far more than upon an increase in the number of beds. Moreover, the increase in population of London has rather been accompanied by an increase in the number of hospitals than in the number of beds at individual hospitals. For these reasons the parallelism between the increase in cancer admissions at The Middlesex Hospital and the increase in the population of London, although interesting, really throws no light upon the problem under consideration.

The importance of the parallelism of the curves dealing with the experience of the Hospital itself is, on the other hand, great, because it is an indication of what one may call "a uniformity of policy" on the part of the Hospital authorities. It indicates, further, that the reputation of The Middlesex Hospital for the treatment of cancer has not undergone great variations, and

that any improvement in diagnosis of cancer has been at least equalized by improvements of diagnosis in other diseases. In an enquiry in which there are so many possible variables as there are in the present, it is impossible to over-estimate the value of such constants.

The depressions in the General Admission Curve during the years 1876—78, 1887, 1893, and 1898 were due to partial closing of the Hospital for cleaning, building, and repairs.

C.—*The Percentage Mortality from Carcinoma in the Age* 35 *Populations, compiled from the Records of The Middlesex Hospital.*

At the commencement of this Paper reasons were given for concluding that it was possible to form populations of healthy persons, aged 35 years, of each member of which the cause of death is known. It is with these populations that the following section is concerned. Table III. shews the percentage borne by the deaths from cancer to the total number of deaths in the population of each year. This Table is deduced from Table I. From it curves have been drawn shewing the same facts graphically (Plate VI.). The portions of the curves in red ink are hypothetical, and will be considered later.

The first striking fact from these curves is that the curve for females is much higher than that for males. This point might have been anticipated from the statements already made on page 136, which shew that out of a population of 6,000 males the experience of The Middlesex Hospital is that 2,000 die of carcinoma, whereas, out of the same number of females, carcinoma accounts for a mortality of 4,000.

From our present point of view, however, the most important facts shewn by the curves are: (1) There has been a progressive increase in the percentage mortality from carcinoma from about the year 1830 to about the year 1875, and (2) this progressive increase in percentage mortality from carcinoma affected both sexes alike.

So far as concerns the period up to the year 1864, the curves present no difficulty in reference to the question now under discussion, but it will be noticed that from about the year 1880 there has been a rapid fall in the two curves. The explanation

TABLE III.

Percentage Cancer Mortality in the Age 35 Populations, Compiled from The Middlesex Hospital Records.

Age 35 Population of the Year	Percentage Mortality from Carcinoma.		Age 35 Population of the Year	Percentage Mortality from Carcinoma.	
	Male.	Female.		Male.	Female.
1814	25·0	66·6	1858	30·8	58·1
1815	40·0	12·5	1859	30·6	70·5
1816	28·6	16·6	1860	33·1	74·8
1817	20·0	16·6	1861	38·3	66·1
1818	23·1	20·0	1862	31·5	56·2
1819	40·0	33·3	1863	48·5	74·0
1820	15·4	30·8	1864	31·1	60·4
1821	9·1	60·0	1865	25·9	71·9
1822	16·6	25·0	1866	31·5	70·7
1823	36·4	36·4	1867	32·5	69·0
1824	41·2	47·4	1868	37·1	69·0
1825	38·1	35·7	1869	33·3	67·2
1826	16·6	40·0	1870	50·0	79·1
1827	11·7	50·0	1871	40·0	69·2
1828	25·0	41·2	1872	37·2	68·0
1829	34·7	31·0	1873	37·8	71·7
1830	6·9	48·3	1874	30·8	68·0
1831	16·6	40·9	1875	38·8	72·8
1833	28·6	46·7	1876	36·6	71·8
1833	27·8	40·0	1877	36·7	75·4
1834	20·0	33·3	1878	45·1	70·1
1835	29·4	42·1	1879	40·4	79·3
1836	16·6	26·9	1880	47·7	66·9
1837	24·0	44·7	1881	46·1	70·4
1838	24·2	66·6	1882	44·9	73·7
1839	20·9	46·9	1883	42·7	63·3
1840	16·9	60·0	1884	49·4	78·3
1841	26·9	59·1	1885	34·6	66·6
1842	22·5	47·2	1886	43·4	63·4
1843	20·9	53·3	1887	30·8	60·0
1844	27·2	62·5	1888	32·3	73·8
1845	20·4	60·2	1889	25·5	70·2
1846	27·1	65·1	1890	22·7	66·1
1847	23·7	54·8	1891	23·9	56·9
1848	22·5	62·1	1892	36·2	62·9
1849	24·3	58·3	1893	24·3	59·0
1850	28·6	54·9	1894	25·0	66·6
1851	30·6	55·4	1895	34·3	38·9
1852	21·7	55·0	1896	18·2	57·7
1853	26·4	61·0	1897	16·7	67·6
1854	31·6	55·6	1898	33·3	26·7
1855	30·9	63·2	1899	27·3	55·6
1856	30·3	61·1	1900	10·0	33·3
1857	37·6	56·5			

of this fall is simple. It is clear that a person aged 35 in the year 1880 is only 59 years of age in the present year (1904), and therefore there is a complete lack of all lives above that

age in the population for 1880. Consequently, since we are dealing with ages up to 75, the populations are only absolutely complete up to the year 1864. If we had records up to the year 1941, then all persons aged 75 in 1900 would be included. In order, therefore, to arrive at a conclusion with regard to the latter parts of the curves, these lacunæ must be filled up by means of figures derived from an average. Further, the data already at hand for years before 1904 will, if added to the figures obtained from an average, impress their own characters upon this average. Now a person 35 years of age in 1864 is only *now* (in 1904) 75 years of age. Consequently our age 35 population in 1865 is deficient by reason of the lack of persons age 75, for they will not be 75 years until 1905. Similarly, our age 35 populations in 1866 do not reach 75 years until 1906, and are deficient because they lack ages 74 and 75, and so on.

Consequently if—

a =	average	number	of	persons	dying	yearly	of cancer	at age 75,
A =	,,	,,	,,	,,	,,	non-cancer	,,	,,
b =	,,	,,	,,	,,	,,	cancer	,,	74,
B =	,,	,,	,,	,,	,,	non-cancer	,,	,,
c =	,,	,,	,,	,,	,,	cancer	,,	73,
C =	,,	,,	,,	,,	,,	non-cancer	,,	,, etc.

Then—

a	has to be added	to	the	observed	cancer	figures in year 1864,
A	,,	,,	,,	non-cancer	,,	,,
a + b	,,	,,	,,	cancer	,,	1865,
A + B	,,	,,	,,	non-cancer	,,	,,
a + b + c	,,	,,	,,	cancer	,,	1866,
A + B + C	,,	,,	,,	non-cancer	,,	,, etc.

In order to arrive at the values to be given to a, A, b, B, c, C, etc., the records of the three years 1895, 1896, and 1897* were re-examined, and all cases, cancerous and non-cancerous, dying above the age of 35 years (or included with those according to the lines on which the statistics were drawn up throughout the investigation) were collected. These were then

* It was considered safer to take a period of years towards the end of the century, than to take the average of the entire series of records from which our cases were derived, since the probability is that the year 1940 will differ less from the year 1895 than from the year 1845 for example.

arranged according to their ages at death, and gave the following averages for each sex :—

TABLE IV.

The Middlesex Hospital Yearly Average Mortality from Cancer and Non-Cancerous Diseases between the ages 35 and 75.

Males.			Females.		
Age.	Cancer.	Non-Cancer.	Age.	Cancer.	Non-Cancer.
35	·3	2·3	35	3·0	·6
36	·6	1·3	36	2·3	1·6
37	0	1·6	37	2·3	1·0
38	2·3	·3	38	3·6	2·0
39	·3	3·0	39	4·0	1·3
40	·3	·6	40	2·6	2·6
41	·6	2·0	41	2·0	·6
42	1·3	2·3	42	3 3	2·0
43	·6	1·6	43	4·6	1·3
44	1·6	1·6	44	4·6	1·0
45	3·0	1·6	45	4·6	3·3
46	2·0	1·6	46	5·0	1·0
47	2·3	·3	47	4·0	1·3
48	1·6	1·3	48	4·6	1·6
49	2·0	1·3	49	4·0	1·3
50	3·3	1·3	50	6·3	1·3
51	2·0	·6	51	3·6	·6
52	3·6	·6	52	4·3	0
53	2·0	2·0	53	5·3	·3
54	3·0	1·6	54	4·6	·6
55	1·6	2·0	55	5·6	1·0
56	1·6	1·6	56	3·3	1·0
57	1·3	1·6	57	3·0	1·3
58	2·3	2·0	58	6·6	·6
59	1·6	0	59	3·0	0
60	3·3	1·0	60	5·0	4·6
61	1·6	·6	61	1·6	1·3
62	2·3	1·6	62	2·6	1·0
63	1·6	1·6	63	4·0	·6
64	2·6	1·3	64	3·3	1·3
65	2·3	·3	65	3·3	·6
66	1·0	1·6	66	1·0	·3
67	·6	1·3	67	3·6	·6
68	1·3	·6	68	·6	·3
69	1·6	·3	69	·6	·3
70	1·3	1·3	70	2·3	1·6
71	1·0	1·0	71	·3	1·0
72	2·0	0	72	1·0	·6
73	1·0	·3	73	2·0	·3
74	1·3	0	74	0	0
75	·6	1·3	75	·3	·3

Taking then these averages and constructing a hypothetical series of records reaching to the year 1941, it becomes necessary to add the figures in Table V. to the ascertained figures (Table I.)

from the year 1864 onwards, in order to obtain populations in all years between the ages of 35 and 75. With these combined figures percentages have been made similar to those obtained (TABLE III.) for the earlier parts of the curve, and the modified curves thus produced are printed in red ink.

TABLE V.

Estimated Figures to be added to ascertained Figures, and Percentages deduced therefrom, in order to complete the Age 35 *Populations* (*Middlesex Hospital*) *up to Age* 75 *in the year* 1900.

	MALES.			FEMALES.		
Year.	Cancer.	Non-Cancer.	Corrected Percentage.	Cancer.	Non-Cancer.	Corrected Percentage.
1864	1	1	31·4	0	0	60·4
1865	2	1	26·7	0	0	72·0
1866	3	2	32·6	2	1	70·7
1867	5	2	36·7	3	1	69·2
1868	6	3	39·0	4	2	68·2
1869	7	4	35·7	6	4	66·6
1870	9	4	52·0	7	4	78·1
1871	10	5	42·9	7	5	68·4
1872	11	6	39·9	11	5	68·1
1873	12	8	41·0	12	6	71·2
1874	14	8	36·4	15	6	68·5
1875	17	10	42·5	19	8	72·4
1876	19	11	41·6	23	9	71·8
1877	21	13	43·2	25	11	74·1
1878	23	14	49·3	27	15	68·4
1879	26	15	46·7	32	15	75·6
1880	28	15	51·9	35	16	67·5
1881	30	17	52·2	42	17	70·7
1882	31	18	52·0	45	18	72·2
1883	33	20	50·4	48	19	67·1
1884	35	22	54·1	54	20	75·8
1885	38	24	46·4	58	20	70·1
1886	40	26	51·0	64	20	69·2
1887	43	26	42·2	68	21	68·5
1888	45	27	48·2	72	22	75·3
1889	49	28	47·7	78	24	74·2
1890	51	30	48·8	82	25	72·8
1891	52	31	48·8	87	27	70·3
1892	55	31	54·1	91	28	71·8
1893	57	33	52·0	96	31	71·7
1894	60	35	51·9	100	32	74·1
1895	61	36	55·3	105	33	71·9
1896	62	38	51·1	110	35	73·1
1897	63	40	52·8	113	36	74·3
1898	64	42	56·5	115	39	70·4
1899	64	43	56·8	118	40	72·7
1900	65	46	54·5	122	42	72·5

In considering the two portions of the two curves (Plate VI.) from 1864 to 1900, the practical identity of the corrected and the uncorrected portions up to about the year 1885 is clear. This depends upon the fact that persons age 35 in 1885 are *now* age 59, and therefore are at about the period of greatest incidence of cancer. Hence previous to that date the greater proportion of the cases have actually been recorded. On closer examination of the curves it appears that the correspondence of the curves extends later in the case of females than in the case of males. The explanation of this lies in the fact that the age of maximum incidence of carcinoma is about five years later in the male than in the female.*

From about the year 1885 there occurs an increasing divergence between the corrected and uncorrected portions of the curves, but the divergence is different in the two cases; for whereas the corrected curve for females continues onwards in a more or less horizontal direction until it merges into the horizontal straight line, theoretically obtained from populations age 35 derived from a constant yearly incidence of cancer (the average yearly series), the corrected curve for males continues to rise. Thus the curve for females, which rose continuously from 1814 to 1870, from 1870 onwards has been practically horizontal. On the other hand, the curve for males has been one continuous rise throughout.

It is now necessary to consider the actual meanings of these curves. From the method of making them it is clear that the experience of The Middlesex Hospital is that at all events up to about the year 1870 there was in both sexes a gradual increase in the percentage of cancer deaths, and that after this period the percentage cancer mortality in females remains stationary, while in males it continued to rise. This may mean (1) an increase in the number of cases of cancer admitted, the number of cases of disease other than cancer being stationary; (2) a stationary admission for cancer and a diminished admission for non-cancerous diseases; (3) an increase in cancer admissions and a diminished admission for non-cancerous disease; (4) a stationary, increased, or possibly, diminished number of cancer admissions along with a diminished death-rate from non-

* *Cf.* "Archives Middlesex Hospital," Vol. II., 1904 (Second Cancer Report), p. 128.

cancerous disease; (5) a disproportionate increase in the cancer admissions, admissions for all kinds of disease having increased.

Now there is no doubt that admissions for all forms of disease have increased, as is shewn by TABLE II. and PLATE V., and there equally is no doubt that the percentage admission for cancer at The Middlesex Hospital has remained practically stationary. Hence the possibilities (1), (2), and (3) can be summarily dismissed. With regard to the fourth and fifth possibilities the case is different.

Dealing with the possibility that there has been a diminished death-rate of recent years from cancerous disease, it is clear that a large number of persons who formerly died of hospital gangrene, etc., in pre-antiseptic days, may, after the introduction of Listerism, have survived to swell the numbers of those who ultimately died of cancer. But under these conditions it would be expected that the male and female curves should coincide in their directions throughout. It is true that males are more liable to surgical diseases than females, and therefore that the improvements in surgery would diminish the non-cancerous male mortality more than the female. But this would hardly account for so striking a dissimilarity in the latter parts of the curves.

TABLE VI.

Numbers and Percentages of "Surgical" and "Medical" Deaths amongst Non-Cancerous Cases of Age 35 Populations (Middlesex Hospital).

	Male.			Female.		
Year.	Surgical.	Medical.	Surgical Percentage of Total.	Surgical.	Medical.	Surgical Percentage of Total.
1820	5	6	45·5	5	4	55·6
1830	11	16	40·8	7	8	46·7
1840	16	38	29·6	9	17	34·6
1850	23	57	28·7	14	32	30·4
1860	24	59	28·9	7	27	20·6
1870	12	43	21·8	4	20	16·6
1880	14	36	28·0	11	26	29·7
1890	10	24	29·4	6	15	28·6
1900	3	6	33·3	1	5	16·6

Further, there is no inherent probability that a person saved from a "surgical death" by modern surgical methods should

die of carcinoma rather than by a "medical death." In this connection it is important to note that the great majority of the non cancerous deaths in our series have actually taken place in the medical wards from "medical" diseases. That there has been a gradual and definite diminution in mortality amongst surgical cases, in spite of a great increase in the range of surgical operations, our examination of the clinical records of the Hospital clearly shews; but that this factor does not enter largely into the entire question dealt with in the present section is shewn in TABLE VI.

Taking the above series, "medical" deaths form 70·72 per cent. of the entire non-cancerous male deaths, and 70·64 per cent. of the female non-cancerous deaths. Any modern improvement in medical death-rates above the age of 35 years is so small as to be negligible.*

Since, then, (*a*) the great proportion of our non-cancerous cases are medical, and (*b*) the curves for females and for males are not parallel, it is necessary to reject the hypothesis that the directions taken by the curves formed from the ratios between the cancerous and non-cancerous mortality depend upon a diminished death-rate from non-cancerous disease.

Finally, there is the possibility that the characters of the curves depend upon a disproportionate increase in the number of cancer cases.

Amongst the factors which might increase the number of cases of carcinoma admitted to Hospital, reference has already been made to increase of population, and it has been shewn that this cannot be regarded as explaining the observed facts. So, too, the possible effects of improved methods of transit, increased facilities for reaching the Hospital, improved education, etc., in the different decades have been completely eliminated by the method of forming populations at one age. The cancerous, non-cancerous, medical, and surgical patients of any one of our populations have been placed, practically, under the same conditions in these respects, because they were all of one age at the same time. They may, and undoubtedly do, in part account for the actual increases in the numbers of patients, but

* The improvement in medical mortality has taken place especially in connection with such diseases as are due to improper feeding of infants, diphtheria, tuberculosis, typhoid fever, etc., and chiefly concern persons *below* the age of 35.

they leave the ratios borne by cancerous to non-cancerous admissions untouched.

The view that there has been a definite and disproportionate increase in cancer at The Middlesex Hospital receives further (but indirect) support from a consideration of the ratios obtaining between the cancer admissions and the general admissions. Although the percentage is practically a constant one it is not actually so, a certain small rise having taken place since about the year 1880.

Dealing now with the final parts of the curves, a difficulty arises by reason of the fact that an increasing number of the cases going to the manufacture of the curves is not definitely ascertained, but has been estimated. If it be granted that the ascertained figures impress their own characters upon the theoretical curve formed from the yearly average distribution of cancerous and non-cancerous deaths, then it is clear that the experience of The Middlesex Hospital since about the year 1870 is different in the case of the two sexes.

To sum up, the experience of The Middlesex Hospital with regard to the incidence of cancer is that there was a gradual increase, which affected both sexes, up to about the year 1870, but that since that time the percentage mortality in women has remained stationary, while the percentage mortality in men has continued to increase.

D.—*Age mortality.*

A point of considerable interest was to try and discover whether the mortality from carcinoma at different ages had been the same in persons aged 35 in different decades. In order to do this the cases collected from the statistics were arranged in quinquennial age periods, and in the decades from 1840 to 1900. Thus we were placed in possession of the numbers of persons in these various decades who died from carcinoma between the ages of 35 and 39, 40 and 44, 45 and 49, and so on. These are given in Table VII.

Except in the case of the decades 1840—50 and 1850—60 it is clearly impossible to find the percentage of the total number of cases borne by the actual figures of any quinquennial age period. For although every person age 75 and under who was 35 years of age in either of the decades 1840—50 and

1850—60 has found his place in one or other of the records of the Hospital up to the year 1904, only a certain proportion of those age 35 in the decade 1860—70 have by 1904 reached the age 75, and those the individuals age 35 in either 1861, 1862, 1863, or 1864. Similarly, in still later decades there are greater lacunæ, until in the decade 1890—1900 the only complete number of cases is that which deals with the age quinquennium 35—39.

TABLE VII.

Table shewing the Age Mortality from Carcinoma during the decades 1840—1900 (*Middlesex Hospital*).

FEMALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	9	39	103	85	67	105	53	30
1851-60	53	79	101	129	100	104	75	51
1861—70	65	151	149	189	129	131	90	24* [18]
1871—80	120	160	183	168	166	94* [48]	14* [70]	[56]
1881—90	117	182	169	103* [70]	14* [171]	[167]	[94]	[56]
1891—1900	104	78* [63]	20* [197]	[243]	[217]	[167]	[94]	[56]

MALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	1	12	22	39	40	44	33	23
1851—60	9	17	30	64	42	83	55	49
1861—70	11	41	48	92	81	82	75	28* [23]
1871—80	19	49	79	100	106	76* [33]	15* [56]	[66]
1881—90	23	51	94	82* [41]	42* [70]	[117]	[70]	[66]
1891—1900	29	34* [16]	16* [85]	[140]	[87]	[117]	[70]	[66]

The figures marked with an asterisk are ascertained figures, but are incomplete for the age quinquennia and decades in question, for the same reason as was given on p. 142. The figures printed in square brackets are the estimated figures derived from an average of the years 1895, 1896, and 1897.

In order to complete these lacunæ use was made of the average yearly incidence at different ages, as determined from the actual incidence in each year of age from 35 to 75, during the years 1895, 1896, and 1897 (see TABLE IV., p. 143). According to the number of years constituting the lacuna in any quinquennial age period, a multiple of the average yearly incidence for that age period was estimated. These figures are given in TABLE VII. in square brackets.

To take a specific example. It has already been said that the quinquennial age period 35—39 is complete for the decade 1890—1900. Dealing now with the series of figures for males, our records reaching to 1903 include all persons between 40 and 44 who were 35 years of age in the years 1891, 1892, 1893, and 1894; for the year 1895 we have all persons between 40 and 43; for the year 1896 all persons between 40 and 42; for 1897 persons between 40 and 41; for 1898 all persons at the age 40. But we have no persons at all who were 35 years of age in either 1899 and 1900, and who died at age 40—44, simply because such persons will not reach the ages in question until the year 1905 and onwards. Hence, in completing the figures for the quinquennial age period 40—44 in the decade 1890—1900, it is necessary to add the sum of the *average* numbers dying at the various ages in all the years for which no records are as yet available. In the case given, observed figures were obtained as follows: Age 40, 10 cases; age 41, 5 cases; age 42, 9 cases; age 43, 6 cases; age 44, 4 cases—making 34 cases in all. Estimated figures derived from the yearly average were added as follows: 1 year, age 40 (*i.e.*, 0 case); 2 years, age 41 (*i.e.*, 1 case); 3 years, age 42 (*i.e.*, 4 cases); 4 years, age 43 (*i.e.*, 3 cases); 5 years, age 44 (*i.e.*, 8 cases). The sum of these is 16, and constitutes the figure found in brackets in the third column of the males in TABLE VII. In the quinquennial age period 45—49 the lacunæ are still greater, and the number of actually observed cases is fewer, with the result that the figure estimated after the same method is 85. For the quinquennial age periods from 50 to 74 we have no persons at all who were age 35 in the decade 1890—1900, and so all the figures are in brackets, and are really nothing more than ten times the yearly averages in those quinquennial age periods.

Having thus filled up the lacunæ, the ratios between the total number of persons dying of cancer who were 35 years of age in the various decades and the numbers dying in the various quinquennial age periods were worked out. These are as follows :—

TABLE VIII.

Shewing the Percentages of Deaths at Different Quinquennial Age Periods in the Cancer Deaths of Age 35 *Populations in various Decades* (*Middlesex Hospital*).

FEMALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	1·8	8·0	21·0	17·3	13·7	21·4	10·8	6·1
1851—60	7·7	11·4	14·5	18·5	14·4	14·8	10·8	7·4
1861—70	6·8	16·4	15·7	19·9	13·6	13·8	9·5	4·4
1871—80	11·1	14·8	16·9	15·6	15·4	13·2	7·8	5·2
1881—90	10·2	15·9	14·8	15·1	16·2	14·6	8·2	4·9
1891—1900	8·4	11·4	17·5	19·6	17·5	13·5	7·6	4·5

MALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	·5	5·6	10·2	18·1	18·6	20·5	15·3	10·7
1851—60	2·6	4·9	8·6	18·3	12·0	23·8	15·7	14·0
1861—70	2·3	8·5	10·0	19·2	16·9	17·1	15·6	10·6
1871—80	3·1	8·1	13·1	16·6	17·7	18·1	11·8	10·9
1881—90	3·5	7·8	14·3	18·8	17·1	17·8	10·7	10·1
1891—1900	4·4	7·6	15·3	21·2	13·2	17·7	10·6	10·0

These figures warrant the following conclusions :—

Females.—In the case of women there was an increase in the cancer mortality for the ages 35—39 up to the year 1880, and there was an especially great rise in mortality between these ages in the case of the persons who were 35 years of age during the decade 1870—80. Since that time there has been a gradual diminution in the cancer mortality for these ages. Between the ages 40—44 a considerable rise took place up to 1870, but since that time the mortality has been approximately stationary. There is an indication that a diminution in the mortality is taking place in the case of women 35 years of age during the

decade 1890—1900. Between the ages 45—49 and 50—54 oscillations have occurred, and at the present time there seems to be an increased mortality. Taking the entire series of cases the greatest mortality from cancer in women occurs in the quinquennial age period 50—54; nevertheless the mortality in the age period 45—49 is not much less (16·73 per cent. as against 17·57 per cent.). During the thirty years 1841—70 the mortality from cancer at age 55—59 remained fairly stationary, but a gradual rise has taken place during the thirty years 1871—1900. The cancer mortality at age 60—64 has remained stationary since 1850. And lastly, a gradual diminution has taken place in the cancer mortality between the ages 65—69 and 70—74.

In short, The Middlesex Hospital statistics indicate in the case of women that there is occurring (*a*) a relative diminution in the mortality from cancer between the ages of 35 and 44, and between the ages of 65 and 74; (*b*) a relative increase in the mortality from cancer between the ages of 45 and 59.

Males.—Between the ages of 35 and 39 there has been a steady increase in cancer mortality. For the ages 40—44 a considerable rise took place in respect of the persons who were 35 years of age in the decades 1861—70 and 1871—80; since that time a slight diminution has been occurring. Between the ages 45 and 49 a steady increase in cancer mortality has occurred. In the case of age 50—54 the mortality has been approximately stationary, but there are indications that this is giving place to a rise. Moreover there is evidence that the age of maximum mortality amongst males, which was in the quinquennial age period 60—64 in the case of persons age 35 during the decades 1841—50 and 1851—60, is becoming transferred to the quinquennial age period 50—54; nevertheless, there remains a tendency for an exacerbation of mortality to occur during the age period 60—64. For the age periods 55—59 and 65—69 there has occurred and is occurring a diminished relative mortality. The percentage mortality from cancer for the age period 70—74 remains stationary, or perhaps is undergoing a slight diminution.

In short, The Middlesex Hospital statistics shew that in the case of men (*a*) a steady increase is taking place in the cancer mortality at earlier ages, (*b*) the age of maximum mortality is

becoming younger (50—54), and (*c*) a second rise in mortality occurs during the age period 60—64.

Summary of evidence yielded by the statistics of The Middlesex Hospital :—

In the case of women a steady relative increase took place in cancer mortality up to about the year 1870, but since that time the mortality has remained stationary, although a tendency has shewn itself for a diminution in the mortality during early middle life and old age. This tendency towards diminution, however, has been counterbalanced by a tendency to an increased cancer mortality covering the ages 45 to 59.

In the case of men a steady relative increase in cancer mortality has been taking place from the first, and is still in progress. This increase is associated with an increase in the mortality during the earlier years of middle life, unaccompanied by any noteworthy diminution of mortality in later middle life or in old age.

IV.—STATISTICS OF CARCINOMA FROM ST. GEORGE'S HOSPITAL.

A.—*The Amount of Material.*

The records of St. George's Hospital differ in certain respects from those of The Middlesex Hospital. The post-mortem registers go back to the year 1841, and are of extreme value. The clinical records are complete (admission books and clinical notes) from 1867 ; from 1860 to 1867 only admission books are available. The value of these is obviously much inferior to that of the actual notes, whether clinical or post-mortem, since the diagnoses are entered by the house-officers immediately after admission and before the patient has been under prolonged observation. In spite of this objection the characters of carcinoma, and the fact that only cases of the disease that are at once recognizable are included in our lists, are sufficient to ensure a relatively high degree of accuracy even in this minor portion of the statistics. As in the case of The Middlesex statistics, the greatest care has been exercised in order to avoid the possibility of counting "recurrences" as separate cases.

In all, 13,840 cases have been analyzed, and are included in the figures, tables, and curves presented in the following pages. Of these 9,285 were males and 4,555 females. Of the 9,285

TABLE IX.

Cancerous and Non-Cancerous Age 35 Populations, Compiled from the Records of St. George's Hospital.

Year.	Males.		Females.		Year.	Males.		Females.	
	Cancer.	Non-Cancer.	Cancer.	Non-Cancer.		Cancer.	Non-Cancer.	Cancer.	Non-Cancer.
1801	0	3	0	0	1851	13	127	21	35
1802	0	0	0	3	1852	14	139	25	60
1803	0	2	0	0	1853	13	126	23	53
1804	1	1	0	2	1854	19	174	35	47
1805	0	5	0	3	1855	33	166	20	73
1806	0	3	1	1	1856	30	153	34	71
1807	0	2	0	3	1857	17	151	39	59
1808	0	3	0	5	1858	26	129	28	64
1809	1	5	0	4	1859	22	134	43	57
1810	0	8	0	3	1860	22	142	21	53
1811	0	9	0	3	1861	25	141	27	47
1812	0	5	0	8	1862	38	143	23	56
1813	0	8	0	8	1863	27	122	31	51
1814	2	9	1	4	1864	32	155	21	51
1815	2	11	1	6	1865	37	156	32	67
1816	0	13	0	8	1866	29	148	37	62
1817	1	11	0	3	1867	23	134	25	47
1818	3	18	3	14	1868	19	166	25	61
1819	0	26	2	13	1869	37	135	32	53
1820	2	18	0	10	1870	33	122	27	42
1821	1	24	1	14	1871	35	116	30	45
1822	3	37	3	15	1872	38	139	29	54
1823	1	28	1	11	1873	29	121	31	45
1824	1	42	2	20	1874	27	110	30	49
1825	2	46	2	20	1875	27	140	27	46
1826	4	50	1	15	1876	27	129	39	54
1827	3	47	5	16	1877	29	122	41	35
1828	2	52	1	26	1878	27	106	34	44
1829	2	52	0	28	1879	23	117	35	37
1830	4	58	11	25	1880	27	112	27	39
1831	9	65	3	21	1881	21	94	16	35
1832	4	59	4	27	1882	15	85	32	36
1833	7	69	5	31	1883	20	86	23	31
1834	4	79	8	30	1884	23	99	23	31
1835	9	134	8	39	1885	12	91	17	39
1836	7	100	12	55	1886	10	96	20	37
1837	10	100	6	41	1887	12	67	18	38
1838	10	114	2	29	1888	10	63	16	30
1839	11	112	12	38	1889	9	67	12	22
1840	12	103	15	41	1890	13	62	20	23
1841	9	117	4	32	1891	10	54	17	25
1842	10	110	7	55	1892	12	59	9	19
1843	18	107	11	48	1893	2	50	8	18
1844	10	123	11	54	1894	2	52	17	23
1845	25	134	13	44	1895	7	41	13	13
1846	9	145	20	51	1896	4	33	5	14
1847	14	144	9	52	1897	2	31	3	17
1848	11	121	12	48	1898	1	25	7	7
1849	13	121	16	47	1899	1	22	2	1
1850	12	128	15	57	1900	3	16	5	5

cases in men, 1,236 were cases of carcinoma, and 8,049 cases of disease other than carcinoma. Of the 4,555 female cases, 1,403 were carcinomatous, 3,152 were non-carcinomatous. TABLE IX. gives a full list of the several years, with the number of cases that were accumulated under each.

The total number of cases that were reviewed in order to obtain the figures given above cannot well have been short of about 170,000. Between the years 1870 and 1899 over 115,000 cases were admitted into St. George's Hospital.

B.—*The Ratios borne by the Cancer Admissions to the General Admissions at St. George's Hospital.*

For comparison with a similar Table, drawn up in the previous part of this Paper, the following figures are given :—

TABLE X.

Cancer and General Admissions to St. George's Hospital, 1870—1899.

Year.	Female Cancer Admissions.	Male Cancer Admissions.	Total Admissions to Hospital (both Sexes).	Percentage of Total Cancer Admissions to Total Admissions.
1870	15	15	3683	0·82
1871	19	11	3240	0·92
1872	22	15	3574	1·03
1873	23	16	3736	1·04
1874	10	16	2514	1·03
1875	36	22	3766	1·54
1876	24	22	3549	1·29
1877	30	17	3416	1·37
1878	37	30	3728	1·79
1879	26	27	3796	1·39
1880	30	23	3553	1·49
1881	28	20	3703	1·29
1882	28	28	4000	1·40
1883	37	30	4013	1·66
1884	32	33	4112	1·58
1885	36	31	3883	1·72
1886	24	41	3558	1·82
1887	28	34	3500	1·77
1888	31	25	4365	1·28
1889	35	33	4272	1·59
1890	41	34	4485	1·67
1891	30	38	4112	1·65
1892	28	27	3230	1·70
1893	26	31	4135	1·28
1894	36	40	4205	1·80
1895	37	33	3874	1·80
1896	43	49	3887	2·46
1897	31	42	4404	1·65
1898	39	36	4189	1·79
1899	54	35	4412	2·61

Plate VII. has been drawn from the figures in Table X., in order to present the facts graphically.

In these curves a marked parallelism is observable, although the general admissions rise somewhat more acutely. But little difference is seen between the curves for males and for females when the broad aspects of the curves are considered. The percentage of cancer to general admissions, in spite of variations in different years, is practically a straight line. The importance of this point has already been referred to (p. 139).

C.—*The Percentage Mortality from Carcinoma in the Age 35 Populations, compiled from the Records of St. George's Hospital.*

In Table XI. are given figures and in Plate VIII. is presented a series of curves describing the percentages of the persons in each of our age 35 populations who ultimately died from carcinoma. The portions of the curves in red ink are in a varying degree hypothetical, inasmuch as they are deduced from adding the ascertained numbers to numbers derived from the average incidence of carcinoma in St. George's Hospital during the years 1895, 1896, 1897.

The striking points concerning these curves are: (1) The curve for females is consistently higher than that for males, a point agreeing with the figures given on p. 155, which shew that the experience of St. George's Hospital is that cancer is more than twice as common amongst women as amongst men; (2) There has been a progressive increase in the percentage mortality from carcinoma from about the year 1826 to about the year 1876 for females, and 1871 for males.

With regard to the reasons of modifying the observed figures after the year 1864, the reader is referred to p. 150. Following the plan there described in detail, the figures given in Tables XII. and XIII. were constructed.

In considering the two portions of the two curves (Pl. VIII.), it is clear that from 1864 to about 1886 in the case of females, and 1880 in the case of males, there is practical identity between the corrected and uncorrected portions. The reason for this has already been given (p. 145).

TABLE XI.

Percentage Cancer Mortality in the Age 35 Populations, Compiled from the St. George's Hospital Records.

Age 35 Population of the year	Percentage Mortality from Carcinoma.		Age 35 Population of the year	Percentage Mortality from Carcinoma.	
	Male.	Female.		Male.	Female.
1814	18·2	20·0	1858	16·8	28·5
1815	15·4	14·3	1859	14·1	43·0
1816	—	—	1860	13·4	28·6
1817	8·3	—	1861	15·0	36·5
1818	14·3	17·6	1862	20·9	29·1
1819	—	12·6	1863	18·1	37·8
1820	10·0	—	1864	17·1	29·2
1821	4·0	6·3	1865	19·0	32·3
1822	7·5	16·6	1866	16·4	37·4
1823	3·4	8·3	1867	14·6	34·7
1824	2·3	9·1	1868	10·3	28·6
1825	4·2	9·1	1869	21·5	37·6
1826	7·4	6·2	1870	21·3	39·1
1827	6·0	23·8	1871	23·2	40·0
1828	3·7	3·8	1872	21·5	34·9
1829	3·7	—	1873	19·3	40·8
1830	6·4	30·5	1874	19·6	38·0
1831	12·2	12·5	1875	16·2	37·0
1832	6·3	12·9	1876	17·3	42·0
1833	9·2	13·9	1877	19·2	53·9
1834	4·8	21·0	1878	20·3	43 6
1835	6·3	17·0	1879	16·4	48·6
1836	6·5	17·9	1880	19·4	40·9
1837	9·1	12·7	1881	18·3	31·4
1838	8·1	6·4	1882	15·0	47·1
1839	8·9	24·0	1883	18·9	42·6
1840	10·4	26·8	1884	18·9	42·6
1841	7·1	11·1	1885	11·7	30·4
1842	8·3	11·3	1886	9·4	35·1
1843	14·4	18·6	1887	15·2	32·1
1844	7·5	16·9	1888	13·7	34·8
1845	15·7	22·8	1889	11·8	35·3
1846	5·8	28 1	1890	17·3	46·5
1847	8·8	14·7	1891	15·6	40·5
1848	8·3	20·0	1892	16·9	32·1
1849	9·7	25·4	1893	3·8	30·8
1850	8·6	20·8	1894	3·6	42·5
1851	9·3	37·5	1895	14·6	50·0
1852	9·1	29·4	1896	10·5	26·3
1853	9·4	30·3	1897	6·1	15·0
1854	9·8	42·7	1898	4·0	50·0
1855	16·5	21·5	1899	4·5	66·6
1856	16·4	32·4	1900	15·8	50·0
1857	10·1	40·6			

From the years mentioned there occurs an increasing divergence between the corrected and uncorrected portions, and

the divergence is different in the two cases: for whereas the corrected curve for females tends at first to fall and subsequently takes on a more or less horizontal position, the curve for males continues to rise, although the rise is somewhat more gradual than over the earlier part of the curve (1820—70).

TABLE XII.

The St. George's Hospital Yearly Average Mortality from Cancer and Non-Cancerous Diseases between the Ages 35 and 75.

Males.			Females.		
Age	Cancer.	Non-Cancer.	Age.	Cancer.	Non-Cancer.
35	·3	3·7	35	·6	2·0
36	0	3·3	36	1·0	2·3
37	·3	4·0	37	0	2·3
38	·6	6·0	38	·6	1·3
39	·3	6·6	39	1·6	3·3
40	·6	5·0	40	2·6	2·3
41	1·0	4·0	41	·6	2·3
42	·3	4·3	42	1·6	1·6
43	·6	5·6	43	1·6	1·6
44	·6	2·3	44	1·0	1·6
45	1·0	5·0	45	·3	2·0
46	0	5·0	46	1·3	1·6
47	·3	2·0	47	1·3	2·0
48	·6	2·3	48	2·0	1·0
49	1·6	2·3	49	2·0	1·0
50	1·6	5·0	50	1·3	3·3
51	1·6	4·0	51	1·6	1·0
52	2·6	3·6	52	3·3	1·0
53	2·0	2·6	53	·3	·6
54	1·3	4·0	54	1·0	2·0
55	1·0	3·3	55	1·3	1·0
56	1·6	6·0	56	1·0	0
57	2·0	·6	57	1·0	2·6
58	·3	3·6	58	1·0	1·3
59	2·3	1·0	59	1·3	·3
60	2·6	7·0	60	·6	1·6
61	1·0	5·3	61	1·0	0
62	2·0	3·0	62	·6	1·0
63	·6	4·3	63	·6	1·0
64	2·6	5·3	64	1·6	1·0
65	1·0	3·3	65	1·3	2·3
66	·3	6·3	66	·3	1·6
67	1·0	1·6	67	1·0	·6
68	1·6	2·3	68	·3	1·6
69	2·0	2·3	69	·3	2·0
70	·6	1·3	70	0	·6
71	0	1·3	71	0	0
72	·3	1·6	72	·3	1·3
73	·3	1·0	73	·3	1·0
74	0	2·0	74	0	·3
75	·3	2·3	75	0	1·0

TABLE XIII.

Estimated Figures to be added to Ascertained Figures, and Percentages deduced therefrom, in order to complete the Age 35 Populations (St. George's Hospital) up to the Age 75 in the Year 1900.

	Males.			Females.		
Year.	Cancer.	Non-Cancer.	Corrected Percentage.	Cancer.	Non-Cancer.	Corrected Percentage.
1864	0	2	16·9	0	1	28·7
1865	0	4	18·8	0	1	32·0
1866	1	5	16·4	0	2	36·6
1867	1	7	14·5	1	4	34·2
1868	1	8	10·3	1	4	28·8
1869	2	10	21·4	1	4	37·1
1870	4	12	21·6	1	6	36·8
1871	5	15	23·4	1	8	36·9
1872	6	16	22·8	2	9	33·0
1873	7	23	20·0	3	10	38·2
1874	8	26	20·5	4	13	35·4
1875	10	31	17·8	6	14	35·5
1876	11	36	18·7	6	15	39·5
1877	13	39	20·7	7	16	48·5
1878	14	44	21·5	8	16	41·2
1879	17	51	19·2	9	17	44·9
1880	19	52	21·9	10	18	39·4
1881	19	56	21·1	11	19	33·3
1882	21	56	20·3	12	22	43·1
1883	23	62	22·5	13	22	40·4
1884	24	66	21·2	14	23	40·7
1885	25	70	18·7	15	25	33·3
1886	27	72	18·0	16	25	36·7
1887	30	76	22·7	19	26	36·6
1888	32	80	21·6	21	27	39·4
1889	33	85	21·6	22	31	39·1
1890	35	87	24·4	24	32	44·4
1891	36	90	24·2	26	33	42·6
1892	36	92	24·1	27	35	40·0
1893	36	97	20·5	29	36	40·7
1894	37	102	20·2	29	38	43·0
1895	38	104	23·7	30	40	44·8
1896	38	110	20·4	32	42	39·8
1897	39	114	22·0	33	43	37·5
1898	40	118	22·3	34	46	43·6
1899	40	123	22·0	37	48	44·3
1900	41	130	23·2	38	51	43·4

It is unnecessary to pursue this subject further, for the arguments used and conclusions on pp. 145—8, when discussing The Middlesex Hospital statistics, are equally applicable in the case of those from St. George's Hospital.

To sum up, the experience of St. George's Hospital with regard to the incidence of cancer is that there was a gradual

increase which affected both sexes up to about the year 1870, but that since that time the percentage mortality in women has remained stationary (although it underwent a temporary depression between 1880 and 1890), while the percentage mortality in men has continued to increase.

D.—*Age Mortality.*

The manner in which these Tables have been constructed and the mode of filling up the lacunæ are given in the section dealing with The Middlesex Hospital statistics, and need not again be referred to.

TABLE XIV.

Table shewing the Age Mortality from Carcinoma during the Decades 1841—1900 *(St. George's Hospital).*

FEMALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	9	7	22	29	17	21	14	2
1851—60	16	29	46	46	47	44	26	10
1861—70	24	47	54	43	50	41	29	{ 10* [2] }
1871—80	17	61	78	75	58	{ 34* [16] }	{ 7* [24] }	[6]
1881—90	30	49	71	{ 41* [20] }	{ 7* [45] }	[48]	[32]	[6]
1891—1900	37	{ 45* [21] }	{ 5* [59] }	[76]	[56]	[48]	[32]	[6]

MALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	2	5	6	12	24	29	21	18
1851—60	3	7	11	25	36	53	21	13
1861—70	14	12	35	44	49	56	38	{ 10* [2] }
1871—80	7	44	65	71	66	{ 54* [27] }	{ 7* [51] }	[13]
1881—90	10	34	40	{ 48* [27] }	{ 7* [60] }	[91]	[60]	[13]
1891—1900	13	{ 20* [9] }	{ 11* [31] }	[94]	[73]	[91]	[60]	[13]

The figures marked with an asterisk are ascertained figures, but are incomplete for the age quinquennia and decades in question. The figures printed in square brackets are the estimated figures derived from an average of the years 1895, 1896, and 1897.

TABLE XV.

Table shewing the Percentages of Deaths at different Quinquennial Age Periods in the Cancer Deaths of Age 35 Populations in various Decades (St. George's Hospital).

FEMALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	7·4	5·7	18·2	23·9	14·05	17·3	11·5	1·6
1851—60	6·06	10·9	17·4	17·4	17·8	16·6	9·1	3·8
1861—70	8·05	15·7	18·1	14·4	16·7	13·7	9·7	3·3
1871—80	4·5	16·2	20·7	19·9	15·4	13·3	8·2	1·6
1881—90	8·5	14·04	20·3	16·2	13·8	13·7	9·1	1·7
1891—1900	9·6	17·1	16·6	19·7	14·5	12·4	8·3	1·6

MALES.

Decade.	Age 35—39	Age 40—44	Age 45—49	Age 50—54	Age 55—59	Age 60—64	Age 65—69	Age 70—74
1841—50	1·7	4·2	5·3	10·6	21·2	24·7	17·9	16·5
1851—60	1·7	4·1	6·5	14·8	21·3	31·3	12·4	7·7
1861—70	5·3	4·6	13·4	16·9	18·8	21·5	14·6	4·6
1871—80	1·7	10·8	16·05	17·5	16·3	20·0	14·3	3·2
1881—90	2·5	8·7	10·2	19·1	17·1	24·3	15·3	3·3
1891—1900	3·1	6·9	10·1	22·6	17·5	21·9	14·4	3·1

The above figures warrant the following conclusions:—

Females.—There is a slight increase in the cancer mortality for the ages 35—39 up to the year 1900, excepting for a fall in the decade 1871—80. Between the ages of 40 and 44 the increase has been continuous up to 1900, save for a fall in the decade 1881—90. Between 45 and 49 the cancer mortality was fairly stationary over the first thirty years. In the decade 1871—80 a rapid rise took place, which was maintained in the succeeding decade, but gives place to a considerable fall in the decade 1891—1900 upon the *purely hypothetical* figures dealing with this age. Age 50—54 shews a considerable diminution over the early part of the period; later, however, a rise is recognizable. Age 55—59 shews a fairly regular diminution from the decade 1851—1860. Ages 60—64, 65—69, 70—74 shew a more or less consistent, though slight, diminution.

In short, the St. George's statistics indicate that in the case of women there is occurring (*a*) a relative increase in the

mortality from cancer between the ages of 35 and 44; (*b*) a relative diminution in the cancer mortality between the ages of 60 and 74; (*c*) taking the age period 50—59, the cancer mortality has been remarkably constant, except during the decades 1861—70 and 1881—90, when there were diminutions.

Males.—In the case of men the cancer mortality between the ages of 35 and 39 has oscillated, but during the last two decades has shewn a tendency to increase, a remarkable percentage being obtained in 1861—70. Between 40 and 49 the cancer mortality steadily increased from 1841—80, but has been diminishing during the last two decades. Between 50 and 54 there has been a steady increase in the mortality from cancer throughout the six decades under consideration. For the quinquennial age period 55—59 the cancer mortality has diminished, although a slight tendency to a rise appears to have shewn itself since the decade 1871—80. Between the ages of 60 and 74, in spite of oscillations, there appears to be a tendency to a diminution in the cancer mortality.

In short, the St. George's Hospital statistics shew: (*a*) that the age of maximum mortality from carcinoma in males is becoming younger (50—54); (*b*) a second rise in mortality occurs during the age period (60—64); (*c*) in spite of oscillations, an increase in the cancer mortality is taking place at earlier ages.

V.—COMPARISON OF THE MIDDLESEX AND THE ST. GEORGE'S STATISTICS.

It is not our intention here to make a detailed and critical examination of the various sets of data derived from the two Hospitals. This work must be left for a future occasion. Certain broad conclusions may, however, be drawn.

The most striking point with reference to the entire series of cases is the great concordance between the results obtained from both Hospitals.

That there should have been over a period of but little less than a century any sort of concordance would in itself have been not only interesting but also suggestive. But when we find that the course of events has been practically identical at the

two Hospitals, and in the case of each sex individually, the argument that each set of data affords reliable information is enormously strengthened.

It is true that the curves from St. George's Hospital are more irregular than those from The Middlesex Hospital; it is true that the years in which the maximum incidence of cancer mortality occurred are not absolutely identical; it is true that the upward rise of the curves from The Middlesex Hospital is more sharp than obtains in the case of the St. George's curves. But when we are enabled to say that the experience of both Hospitals in the case of females is that the cancer mortality gradually rose up to about the year 1870 and has been stationary since, while we are equally enabled to say that the males at both Hospitals have shewn a persistent rise in cancer mortality throughout, each pair of concordant facts lends additional support to the others, and strengthens the general probability that the experience of each Hospital individually may be applied to the population at large.

Further, the fact that the curves at St. George's Hospital are more irregular than at The Middlesex is hardly astonishing, in view (1) of the much greater number of cancer cases at The Middlesex Hospital,* and (2) of the existence at the latter Hospital of a special Cancer Charity, where patients are kept until death.† Where patients, as at St. George's Hospital, are admitted in practically all cases for *operable* cancer, it is clear that modern improvements in technique, etc., tend to produce a greater fluctuation in numbers than where they are partly operable and partly inoperable, as at The Middlesex. The inoperable cases, so to speak, act as ballast.

In reference to the age mortality from cancer, concordance is not so great, although still considerable. Both Hospitals agree that the tendency is for cancer to affect persons—whether males or females—at an earlier age than formerly. Both Hospitals agree that a general diminution in incidence in old age has taken place. Both Hospitals agree that in the case of males the maximum incidence at age 50—54 is followed by a

* Roughly speaking, The Middlesex Hospital has two-and-a-half times as much cancer as St. George's Hospital.

† At St. George's Hospital four beds are reserved for cancer patients until their death.

considerable fall at age 55—59, and that this is in its turn followed by a rise at age 60—64, which nearly reaches to the level of the actual maximum incidence. On the other hand, the fairly consistent rise in mortality amongst women between the ages of 45 and 59, which was noted at The Middlesex Hospital, is not found in the St. George's Hospital series. Moreover, the mortality amongst women between the ages of 35 and 39, which has been diminishing in the experience of The Middlesex Hospital since the decade 1871—80, has been markedly on the increase according to the experience of St. George's Hospital.

Finally, we would wish to express our hearty thanks to the Authorities of St. George's Hospital for the facilities they have given us in connection with this research. The advantage of obtaining information from another independent Institution can hardly be over-estimated.

Plate V.

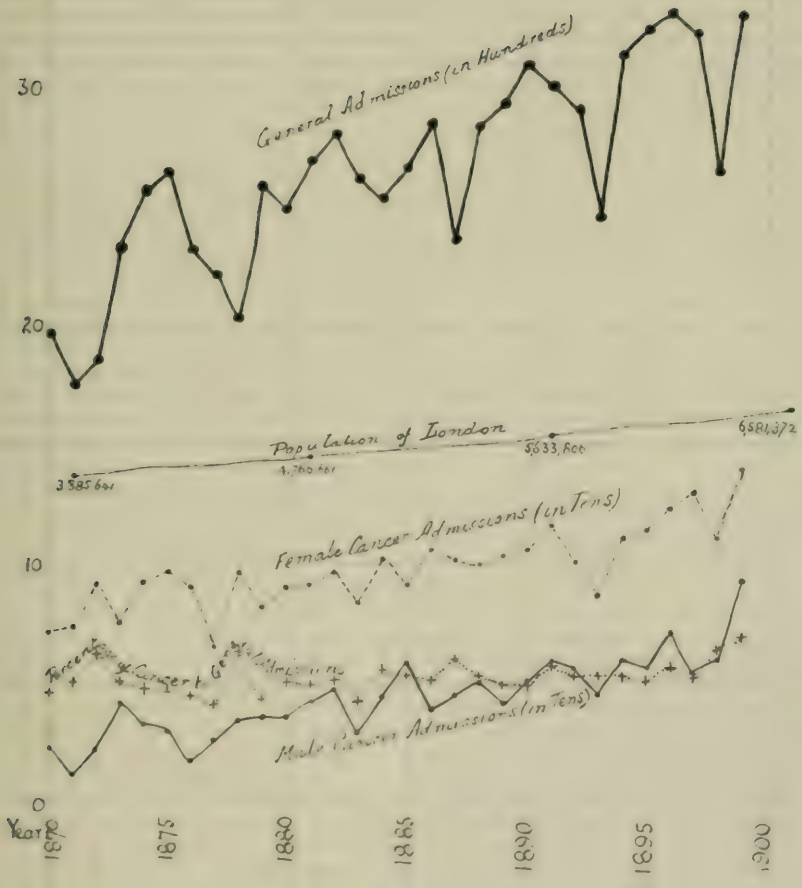

30
20
General Admissions (in Hundreds)
Population of London
3,585,641
4,760,161
5,633,806
6,581,372
10
Female Cancer Admissions (in Tens)
Male Cancer Admissions (in Tens)
0
Year
1870
1875
1880
1885
1890
1895
1900

Plate VI.

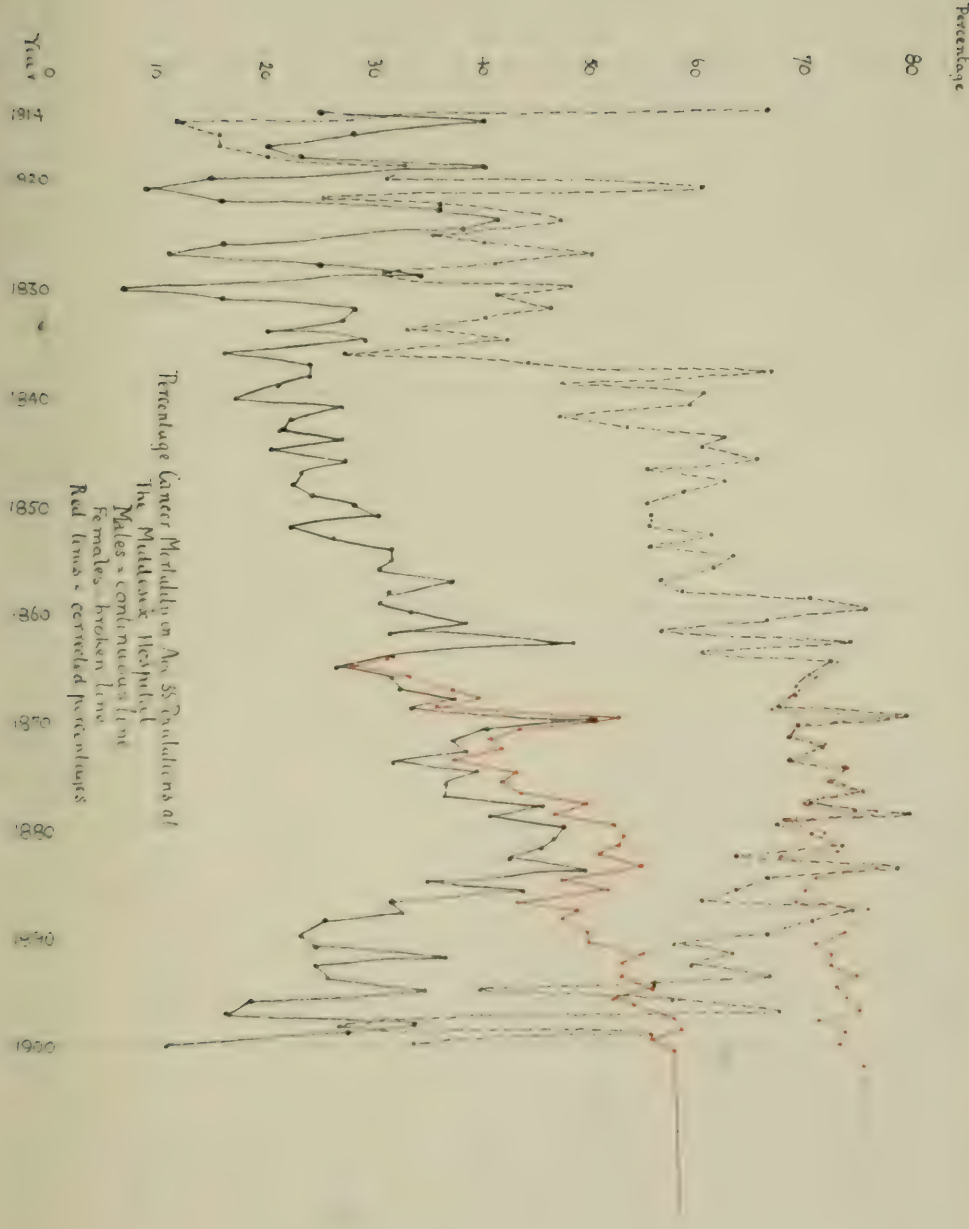

Percentage
0
10
20
30
40
50
60
70
80
Year
1914
1920
1930
1840
1850
1860
1870
1880
1890
1900
Percentage Cancer Mortality on Age 55 Populations at
The Middlesex Hospital
Males - continuous line
Females - broken line
Red lines - corrected percentages

Plate VII.

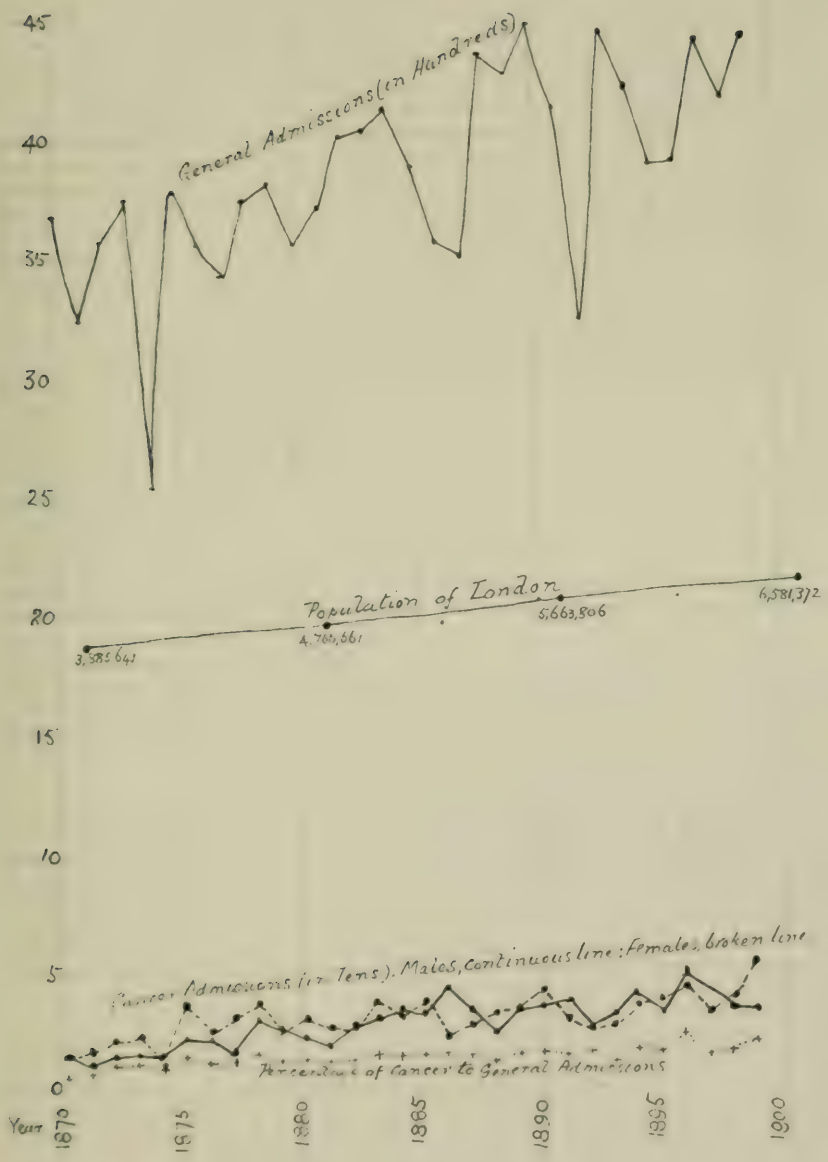
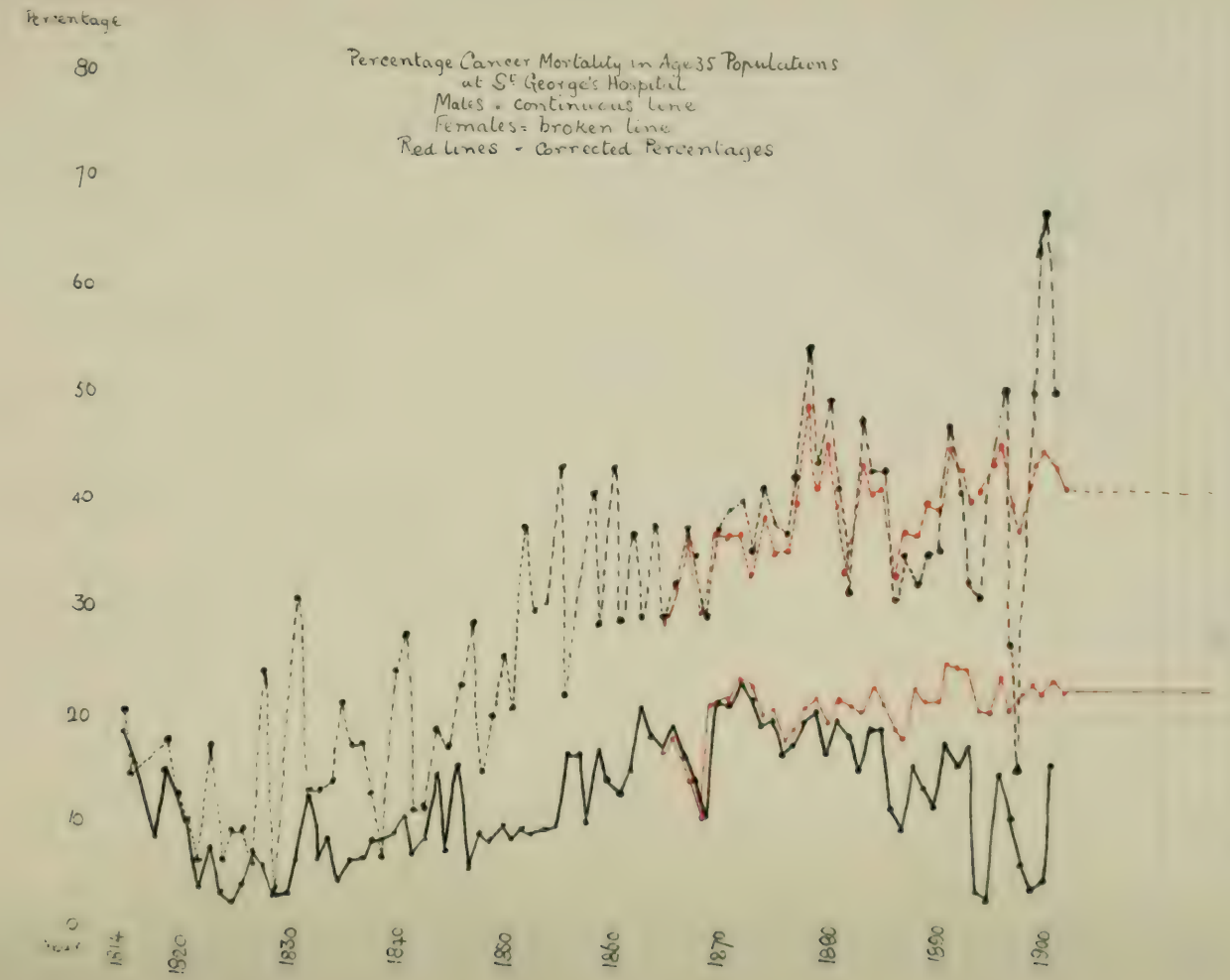

45
40
35
30
25
20
15
10
5
0
General Admissions (in Hundreds)
Population of London
3,585,641
4,766,661
5,663,806
6,581,372
Cancer Admissions (in Tens.). Males, continuous line; Females, broken line
Percentage of Cancer to General Admissions
Years
1870
1875
1880
1885
1890
1895
1900

Plate VIII.


Percentage
Percentage Cancer Mortality in Age 35 Populations
at St George's Hospital
Males - continuous line
Females - broken line
Red lines - Corrected Percentages
80
70
60
50
40
30
20
10
0
1814
1820
1830
1840
1850
1860
1870
1880
1890
1900

ON MULTIPLE PRIMARY MALIGNANT GROWTHS.

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The existence of more than one primary focus of malignant growth in the same patient has been observed and recorded in a certain number of cases, and in some of them the multiple nature of the primary lesions has been demonstrated histologically, and therefore conclusively. At the same time the number of cases is small in proportion to the frequency of the incidence of malignant disease.

During the past four years several cases have occurred in the Hospital and its Cancer Wing, in which double primary growths have been found of different histological type, and several other cases in which multiple growths of similar histological type have been found in what are usually regarded as primary situations, apparently independent of one another, and very closely similar in size.

These cases form the basis of the following Paper, and short protocols of them will be found appended.

Billroth [1] in 1889 enunciated the following criteria, which he regarded as essential to prove the existence of multiple primary lesions :—

(i) The growths must be of different histological structure.

(ii) Each growth must take its origin in normal epithelium of its own type.

(iii) Each growth must produce metastases histologically similar to itself.

M. L. Bard [2] in 1892, in recording a case and discussing those previously recorded, practically adopted Billroth's criteria, while admitting that the third is not an absolutely essential one. He summarily dismissed from consideration the possibility of multiple primary foci of the same histological type.

This view of Bard's seems to have been generally accepted, although recently Morestin [3], while recording an interesting case with two incontestable primary carcinomata of different types, suggests that this view is somewhat too narrow.

It seems to me that since the occurrence of multiple primary lesions, as shewn by different histological features, is an absolutely demonstrated fact, there is *à priori* an even greater probability that two primary growths of the same type should occur. Of course it is at present not possible to prove this incontestably, since the alternative explanation that one of the growths may be secondary either by the usual channels, or by implantation, is very hard to disprove, especially when our lack of knowledge of the conditions determining the site of secondary deposits is taken into consideration. At the same time it must be admitted that cases occur which are explained as easily by the hypothesis of multiple primary deposits, or even more so, than by the above explanations, and therefore the possibility cannot be summarily dismissed without due consideration.

Admitting these general statements, the cases may be conveniently grouped for purposes of discussion as follows:—

I. Cases in which the growths are of different histological type—

(*a*) With an interval between their appearance;

(*b*) When both growths appear approximately simultaneously.

II. Cases in which the growths are of similar histological type—

(*a*) Multiple skin lesions;

(*b*) Multiple lesions in associated organs, or in skin and deeper structures.

I.—(*a*) Multiple Primary Growths with intervals between their appearance.

Cases of this class form a very small proportion of the total cases. Of my own series, Case I. and probably Case II. may be adduced as examples.

It is of interest, though probably a coincidence, that one of my own cases and two of those recorded in the literature have been of the following nature: The first primary growth has

been a squamous-celled carcinoma of the lip successfully treated by excision, followed after some years by a growth in the breast, spheroidal-celled scirrhous carcinoma in two of the cases (both males). The intervals have been, eighteen years in that here recorded (Case I.), fifteen years in Panas' [4] case, and three years in that of Winiwarter [5]. It is worthy of note that in these cases the original growth has been a squamous-celled carcinoma of the lip, a form which is admittedly of a low degree of malignancy in many cases, and therefore offers a greater hope of some duration of life after complete removal. It seems tempting to suppose that if the treatment of cancer by removal in other situations were more generally successful, cases of this class would be more frequently met with; and the second case of my series lends some support to this view, since after successful removal of the breast growth the patient lived six years, developing a second growth in the cervix uteri meanwhile.

If one regards the origin of malignant growths as primarily local, these cases readily admit of explanation on either the view of local irritation, of local embryonic residues, or that of "habit of growth" (Adami).

Such cases have by a few pathologists been regarded as supporting the hypothesis of a cancerous tendency or diathesis. This is, however, hardly tenable considering the long interval which has elapsed in some of the cases.

I.—(*b*) Cases with simultaneous growths of different histological types.

This from most points of view is the most interesting class, since the cases conform to all the criteria necessary to establish multiple primary deposits; and in some cases, as in Case VII. of my series, the distinct histological features of closely adjacent secondary growths in the same organ afford a most excellent demonstration of the conditions.

A point of considerable interest is that among some sixteen cases of this class which I have been able to collect, in seven instances one of the growths was in the alimentary tract, while in two both growths were in that system. In two of the

remaining cases, one of the growths occurred in one of the large glandular outgrowths from the alimentary canal, namely, the liver and pancreas respectively.

Another feature of interest is the frequency with which the association is that of a squamous-celled structure in one growth with a columnar-celled in the other, *i.e.*, both originating in epithelium with protective rather than glandular functions. This, together with the frequency of their occurrence in the cutaneous and alimentary systems, might be taken as possibly indicating an irritation factor in the development of these growths at the same time, since in nearly all cases both growths occur in situations which are usually the site of single primary growths. Too much weight, however, cannot be laid on this consideration. The combinations, moreover, are sufficiently varied, since endothelioma and sarcoma have been recorded as forming one of the original growths, while in Niebergall's case, quoted by Borst ([6]), myomata, polypi, sarcoma, and cancer were present in the same uterus.

With regard to the symptomatology of multiple lesions of this class, the conditions may be obvious when both growths are superficial, but in those cases in which one of the growths is in a deep or internal organ it is very apt to be overlooked during life and only to be found at the necropsy.

So far as I have been able to determine, there does not seem to be any distinct evidence that a greater or more rapid cachexia is induced by multiple growths than occurs in ordinary cases.

II.—(*a*) Multiple Primary Growths in the Skin.

In a certain number of cases of chronic cutaneous irritations, multiple malignant growths appear more or less simultaneously. As examples of this group, it is usual to refer to cases of cancer developing after prolonged administration of arsenic and to cases of occupation-cancer, such as that induced by paraffin, tar, and soot, and to that supervening on senile seborrhœa and Xeroderma pigmentosum. Their chief interest in the present connection is that they lend some support to the existence of the next group.

II.—(*b*) Multiple Primary Growths of Similar Histological Characters.

Three cases have recently occurred which admit of this interpretation. They are Cases IV., V., and VI. of my series.

In discussing the nature and origin of growths of this character, one may admit that there are at least four possibilities.

(1) One of the growths is a secondary deposit produced by the ordinary channels of lymph or blood infection. Against this we have the fact that both growths are found in what are usually primary situations; and although Virchow's dictum that primary sites are infrequent secondary sites is not absolute, yet the occurrence of two constricting growths in the colon, of approximately equal size and development, is a striking coincidence and one that forcibly suggests a separate origin.

(2) That the second growth is an invasion from without by extension from a secondary nodule in a lymph gland in the mesocolon, mesentery, omentum, or elsewhere. On this view, the mucous membrane should be last invaded, and to the least extent, instead of being the most extensively involved, as was the condition in all the cases observed.

(3) The second growth is an implantation of a separated piece of the primary growth on the mucous membrane, as was suggested by Kraske (7) in two cases recorded by him. Admitting the frequency of implantation on serous membranes, its occurrence on mucous membranes is certainly rare; and while this hypothesis explains Kraske's cases quite satisfactorily, since the second growths in the mucous membrane were in both cases small, it is more difficult to accept it for cases in which the size of the two growths is approximately the same, for it would necessitate the supposition that the piece of growth was separated at a time when the original growth was very small, and probably therefore not ulcerated. Again, in Case VI. of my series, the growth at the splenic flexure shewed more marked colloid change than that at the hepatic flexure, suggesting that if anything it was the older growth.

(4) The fourth explanation is that of double primary growth, which is, I submit, at least as probable as the others.

Upon this view primary centres of new growth have appeared in two different situations of similar or closely similar histological features, but quite independently of one another.*

SHORT NOTES OF EIGHT ADDITIONAL CASES OF DOUBLE PRIMARY MALIGNANT DISEASE.

Case I.—*Epithelioma of lip, scirrhus of breast.*

The patient, a male, was operated upon at the London Hospital in 1880, when 66 years of age, for epithelioma of the lip; the growth was not examined microscopically, but was of typical macroscopic characters. In 1898 a mass, the size of a shelled hazel-nut, was noticed under the right nipple. For six months this grew but slightly, although it underwent superficial ulceration, and a reddish offensive discharge came from the nipple. After this the rapidity of growth and extent of ulceration increased, and œdema of the right arm supervened.

On admission to the Cancer Wards in 1900, the patient, though 86 years of age, was of fairly healthy appearance. There was a rough ulcerated growth of two to three inches in diameter in the right mammary region, and the axillary glands on the right side were enlarged.

Death occurred six months later.

Post mortem: There were found a secondary nodule in one of the right axillary glands and a pedunculated polypus of the stomach.

Microscopically the mammary and axillary growths were typical scirrhus; the amount of fibrous tissue in the axillary gland was, however, greater than usual.

* Since the above was written I have read an interesting Paper by Professor v. Hansemann on the simultaneous presence of various different tumours in the same person, in the "Zeitschrift für Krebsforschung," Bd. i., Hft 3, 1904, in which, after referring to a considerable number of additional cases, he critically discusses the whole subject of multiple tumours in a wider sense, including also some non-malignant forms. In the main he arrives at closely similar conclusions to those enunciated above, but he goes further and refers to "unicentric" and "pluricentric" growths, and states that even in some apparently single growths there is histological evidence of pluricentric origin.

CASE II.—*Scirrhus of breast, squamous-cell carcinoma of cervix.*

S. P., female, widow, aged 52. Admitted 14 February 1900.

History: A polypus was removed from the womb at St. George's Hospital in 1893. One half of the left breast was removed in the same Hospital in 1894, the other half being removed at Grantham Cottage Hospital in 1899. The growth was scirrhous carcinoma. During the same year vaginal discharge and pain appeared, and both ovaries were removed at Guy's Hospital. These were healthy.

State on admission: About 1½ inches above the vaginal orifice was a hard ring of new growth ulcerated on the surface; the cervix uteri was hard and deeply ulcerated. The uterus was fixed. There was no sign of recurrence in the left breast.

Death occurred on 17 August 1900.

Post mortem: The cavity of the cervix was large with ragged and sloughing walls, the body of the uterus being invaded, and the bladder and rectum being fixed to the uterus by growth. No other growths were found.

Histologically the growth was probably a squamous-celled carcinoma, but the majority of the cells were small and spheroidal shaped, the central portions of the columns of cells having in many places undergone degeneration.

CASE III.—*Scirrhus of breast, squamous-cell carcinoma of cervix.*

S. B., female, aged 50. Admitted 24 September 1900.

History: The left breast was removed in this Hospital in December 1896.

On admission there was an ulcerated growth of the cervix uteri extending down the posterior vaginal wall, forming masses about one inch across and about one-third of an inch in height. The growth was hard and bled when touched.

Death occurred five months later.

Post mortem: There was growth originating in the cervix and extending into the body of the uterus, which had also invaded the bladder wall. The vagina and rectum were represented by a large cavity with grey sloughing walls, owing to a large recto-vaginal fistula. Secondary growths were found in the inguinal and aortic lymph-glands, liver, lungs, bladder, head of left femur, second lumbar vertebra, and left suprarenal.

There was also some hardness and infiltration of the skin of the left axilla.

Histologically the growth in the breast was a spheroidal-celled carcinoma (scirrhus), that in the cervix was a squamous-celled carcinoma without cell nests, the outermost layer of cells in the epithelial masses being of Malpighian type.

CASE IV.—*Columnar-cell carcinoma of stomach and colon.*

W. A., male, aged 67. Admitted 4 May 1903.

History: The patient was suffering from acute intestinal obstruction, and a growth being found in the descending colon about four inches above the sigmoid flexure during the course of an exploratory laparotomy, left inguinal colotomy was performed. The patient died the same night.

Post mortem: There was an annular carcinoma encircling and greatly constricting the descending colon fourteen inches above the anus. There were a few outlying nodules in the gut wall and adjacent mesocolon. In the stomach, forming a saddle-shaped mass on the lesser curvature a few millimetres from the pylorus, was an extensive mass of new growth, hard and not ulcerated. It had almost encircled the stomach, the greater curvature alone being free. There was an enlarged gland just above the stomach.

Histologically both growths were columnar-called carcinoma.

CASE V.—*Endothelioma of hepatic flexure and transverse colon.*

M. G., female, aged 66. Admitted 8 April 1904.

The patient was a fairly well-nourished woman admitted for pain and vomiting. At an exploratory operation two growths were found, one in the hepatic flexure and one in the transverse colon. Perforation had occurred from stercoral ulceration. Death took place next day.

Post mortem: At the hepatic flexure of the colon there was a constricting growth not quite encircling the gut, but markedly contracting it. The growth was hard and ulcerated, and shewed extensive colloid change. It extended for about one inch along the gut and caused some puckering of the mesocolon and mesentery in its immediate neighbourhood, but it was not adherent to other viscera. About five or six inches

further on in the transverse colon there was a second mass of growth, more extensive in surface but not so thick or so firm as the other growth. It consisted of two extensive patches almost facing one another; the growth apparently started in mucous membrane, and was ulcerated on the surface. The glands in its neighbourhood were involved, one gland on its posterior surface being hard, yellow, and infiltrated. There was stercoral ulceration between the two growths, but no continuity. The glands in the mesentery and mesocolon were invaded by new growth, though this did not shew colloid change. The retro-peritoneal glands were extensively involved, and a large gland was present just above the head of the pancreas, which pressed on but did not invade that organ. Nodules of growth were found in both ovaries and the right suprarenal.

Histological examination: The growth at the *hepatic flexure* was composed of cells often with two or three nuclei, in many instances grouped in lymphatic channels, some parts of section shewing a distinctly lymphangeiomatous appearance. The appearances, though in parts closely resembling a mixed-cell sarcoma, were chiefly those of endothelioma. The growth in the *transverse colon* was of similar character, but even more suggestive of endothelioma.

The metastases failed to shew any differentiation between the two growths though they confirmed the diagnosis of endothelioma.

Case VI.—*Colloid carcinoma of splenic and hepatic flexures.*

W. B., male, aged 50. Admitted 5 April 1904.

The patient was admitted with acute intestinal obstruction, and at the operation a growth was found at the hepatic flexure of the colon, quite fixed. After puncturing the small intestine to relieve distension, a loop of ileum was joined to the transverse colon. Death occurred shortly afterwards.

Post mortem: At the hepatic flexure there was a malignant ulcer, almost encircling the bowel, the edges of which were indurated and everted, while the base of the ulcer presented a warty appearance. A little lower down the gut there was a small polyp, the size of a raspberry, the pedicle of which was about half an inch in length. The splenic flexure of the colon was occupied by a second ulcer which completely surrounded

the bowel, and narrowed its lumen so that it would only admit the tip of the little finger with difficulty. The ulcer had raised and everted edges and its base was ragged and granular. It extended about $1\frac{3}{4}$ inches along the bowel. No secondary growths were found.

Histologically, the growth at the *splenic flexure* was (doubtfully) spheroidal-celled carcinoma. It had, however, undergone complete colloid degeneration, so that a certain diagnosis was impossible. The growth at the *hepatic flexure* was a columnar-celled carcinoma which had superficially undergone colloid degeneration. The polypus was a pedunculated mass of columnar-celled carcinoma.

Case VII.—*Cystadenoma of ovary, squamous-cell carcinoma of cervix uteri.*

S. S. C., female, aged 50. Admitted 20 April 1904.

Vaginal hysterectomy was performed at the London Hospital for carcinoma of cervix uteri in July 1902.

State on admission: The whole pelvic floor was occupied by new growth, which was ulcerated in places, but which constricted the lumen of the rectum. Death occurred on 8 May.

Post mortem: The pelvis was occupied by a mass of new growth which pressed on but did not occlude the rectum. The mass was adherent to the pelvic wall all round and broke down on the slightest pressure. No trace of the ovaries could be found. The floor of the pelvis was involved in the mass, which had ulcerated into the vagina. The terminal coils of the ileum, the cæcum, appendix, and the pelvic colon were all matted together and firmly adherent to the bladder, which was converted into a mass of new growth. The liver contained a few small nodules of growth on its anterior surface, each about the size of a pea, and the substance of the organ was riddled with masses of new growth, more especially the right lobe.

There were deposits in the spleen, the left kidney, both suprarenals, the right lung, the thoracic duct, and the lumbar glands.

Histologically the condition was a mixed one. Squamous-celled carcinoma was present in some parts, while in others ducts lined with columnar cells were found, which suggested a

proliferating cystadenoma of the ovary rather than a columnar-celled carcinoma; over a considerable portion of the primary mass these two types of growths were interlaced. In the liver separate metastases were found, each of which was composed of only one of the two types of growth. It was impossible to decide definitely, but a cystadenoma of the ovary and a squamous-celled carcinoma of the cervix uteri would explain the appearances.

CASE VIII.—*Cystadenoma of both ovaries, columnar-cell carcinoma of colon.*

A. M., female, aged 54. Admitted 2 June 1904.

A middle-aged woman admitted for intestinal obstruction, who died shortly after admission.

Post mortem: At the splenic flexure there was a complete circular growth, soft and ulcerated, constricting the bowel. The uterus contained three fibroids. The right ovary was enlarged by a mass of growth, cystic in places, measuring $16 \times 10 \times 10$ centimetres. The left ovary was similar in character but smaller, measuring $10 \times 7 \times 7$ centimetres. There was one nodule of secondary growth in the liver in the centre of the right lobe and another at the extreme end of the vermiform appendix.

Histologically the *right ovary* closely resembled a columnar-celled carcinoma, but in many features it conformed rather to the type of a cystadenoma. The *left ovary* presented similar appearances, but with more intertubular stroma.

The growth in the splenic flexure was a fairly typical columnar-celled carcinoma with some resemblances to the ovarian growth, but some differences. The growth in the appendix was identical with that in the ovary. The appearances of the nodule in the liver were intermediate between those of the intestine and ovaries, but perhaps more resembled the latter.

[TABLE.

Table of Cases of Double Primary Lesions.

Author's Name.	First growth.	Histological character.	Second growth.	Histological character.
Lannois et Courmont [8]	Œsophagus	Squamous-celled carcinoma ..	Ampulla of Vater in duodenum	Columnar-celled carcinoma.
Orth [9]	Stomach (pylorus) ..	Columnar-celled carcinoma ..	Cæcum	Colloid carcinoma.
Cordes [10]	Stomach	,, ,, ..	Foot	Squamous-celled carcinoma.
Kretz [11]	Dura mater	Endothelioma	Œsophagus	,, ,,
Beck [12]	Cervix uteri	Squamous-celled carcinoma ..	Sigmoid flexure ..	Columnar-celled (gelatinous).
Israel [13]	Tongue	,, ,, ..	Jejunum	Columnar-celled carcinoma.
Kaufmann [14]	* Eyelid (probably Meibomian glands)	Spheroidal-celled carcinoma ..	Rectum	,, ,,
Bard [15]	Cervix uteri	Squamous-celled carcinoma ..	Pancreas	,, ,,
Michelsohn [16]	Nose	,, ,, ..	Breast	Spheroidal-celled (gelatinous).
Panas [17]	Lip	,, ,, ..	,, ...	,, (scirrhus).
Winiwarter [18]	,, ...	,, ,, ..	,, ...	"Cancer."
Morestin [19]	Nipple	,, ,, ..	,, ...	Spheroidal-celled (scirrhus).
Hanot [20]	Liver	"Cancer"	Uterus	"Sarcoma."
Tixier [21]	Larynx	Squamous-celled carcinoma of Malpighian type	Thyroid	Spheroidal-celled carcinoma.
Young	Lip	Squamous-celled carcinoma ..	Breast	,, (scirrhus).
,, ...	Breast	Spheroidal-celled (scirrhus) ..	Cervix uteri	Squamous-celled carcinoma.
,, ...	,, ...	,, ,, ..	,, ...	,, ,,
,, ...	Stomach	Columnar-celled carcinoma ..	Colon (descending) ..	Columnar-celled carcinoma.
,, ...	Colon (hepatic flexure)	Endothelioma	,, (transverse) ..	Endothelioma.
,, ...	,, ,,	Columnar-celled carcinoma ..	,, (splenic flexure)	Colloid carcinoma, ? spheroidal-celled.
,, ...	Ovary	Cystadenoma	Cervix uteri	Squamous-celled carcinoma.
,, ...	Both ovaries	,, ...	Colon (splenic flexure)	? Columnar-celled carcinoma.

* Note.—Was this possibly a rodent ulcer? It is a fact of interest, bearing in mind the chronic course run by rodent ulcer, that I can find no record of the association of another growth with rodent ulcer.

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THE CYTOLOGY OF PAPILLIFEROUS OVARIAN CYSTS.

(Preliminary Communication.)

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Introduction.

The researches of Farmer, Moore, and Walker on the cytology of malignant new growths, and the subsequent publication of similar investigations carried on by Bashford and Murray, have established the important fact that the essential cells of these neoplasms frequently exhibit a method of mitotic division similar to that which obtains in the formation of the gametic cells of animals and higher plants.

A short time after the publication by Farmer and his colleagues of their observations I commenced an investigation into the cytological characteristics of ovarian cysts, both innocent and malignant, with special reference to the papilliferous varieties.

The importance of this last group of tumours from the cytological standpoint is very great, seeing that in them is met every grade of epithelial activity between frank innocency and undoubted malignancy. Amongst them are met some of the most malignant tumours affecting human beings; others shew a partial malignancy, tending to local but not to generalized recurrences; whilst a further group is constituted by those interesting cases in which extensive secondary peritoneal transplantations spontaneously disappear after the removal of the primary growth.

These cases, then, offer a unique field for cytological research whereby it should become possible to define the point at which

the peculiar change in the method of nuclear division characteristic of malignancy first makes its appearance, and possibly the reasons for such a change.

Somatic Division.

One may begin by briefly recalling the normal phases of mitotic cell division as exhibited in all cells dividing indirectly (with the single exception of generative or gametic cells) and known as "somatic mitosis."

The earliest change observable is an accumulation of chromatin in the cell nucleus, whereby it stains more deeply than in the resting condition.

The chromatin now arranges itself within the nuclear membrane in the form of a long, coiled, and continuous thread which exhibits on high magnification an appearance of being formed of two longitudinally arranged rows of chromatin granules.

About this time, or even earlier, two minute bodies known as centrosomes* become apparent, lying usually in the cytoplasm of the cell body outside the nucleus.

They are surrounded by a portion of the cytoplasm more dense than elsewhere and known as the "attraction sphere" or "archoplasm."

This phase (Plate IX., Fig. 2) is called the Prophase.

The two centrosomes now separate, passing to opposite sides of the nucleus, and certain cytoplasmic rays become very conspicuous between them, presenting the shape of a spindle.

The single though convoluted chromatin thread now breaks up by transverse division into a number of small curved portions of approximately equal length (chromosomes).

The number of chromosomes is remarkably constant in any given species. In man, according to Farmer, Moore, and Walker, it is 32.

By this time the nuclear membrane has disappeared, and the chromosomes become bent into a series of V-shaped rods, and in this condition arrange themselves across the equatorial (or mid-transverse) plane of the spindle.

* Centrosomes may be intra-nuclear or even undetectable in certain animals and plants.

They arrange themselves in such a way that the apex of the V-shaped chromosome is directed towards the central point of the spindle, the rest of the V being in the equatorial plane and at right angles to that of the axis of the spindle.

This phase is known as the "early metaphase" or "amphiaster" (PLATE IX., Fig. 3).

Each chromosome now begins to split along the line previously indicated by the double row of chromatin granules, and thus the number of chromosomes is doubled. The half chromosomes thus formed gradually migrate along the lines of the spindle figure towards the centrosomes, each half chromosome passing towards the centrosome nearest to it.

This phase is known as the "late metaphase" or "diaster" (PLATE IX., Fig. 4).

Arrived at their respective poles the chromosomes proceed to rearrange themselves and by aggregation form the nuclei of the new daughter cells.

Indications of the spindle figure still remain at the point where the division of the cytoplasm is about to take place.

This phase is known as the "anaphase" (PLATE IX., Fig. 5).

The cell body now divides at right angles to the axis of the remains of the spindle, a few of whose threads persist for some time and connect the two daughter cells.

This stage is known as the "telophase" (PLATE IX., Fig. 6).

It will be seen therefore that each daughter cell contains the same number of chromatic elements as was possessed by the mother cell.

Heterotype Division.

In gametic cells, however, a form of division occurs which results in each daughter cell having only half the number of chromosomes possessed by the mother cell.

This method of mitotic division is known as "heterotype," and the stages are as follows:—

In early prophase the nucleus is seen to be exceptionally large, the nuclear skein to be very fine and complicated in arrangement. The existence of a double row of chromatic granules in the thread-work is very apparent, a definite though

partial longitudinal splitting being observed throughout the length of the chromatin thread (Plate IX., Figs. 7 and 8).

Later the thread becomes thicker and contracted up towards one point in the periphery of the nucleus forming the *first synaptic figure* (Moore) (Plate IX., Fig. 9).

An opening out of the thread then takes place, causing it to assume the form of long loops arranged on the periphery of the nucleus.

Subsequently a second contraction occurs, the thread undergoing another polarisation to one side of the nucleus (forming the *second synaptic figure*), after which it breaks up by transverse division into chromosomes assuming the form of oval or round rings (Plate IX., Fig. 10). These number only half as many as the somatic chromosomes, and in this ring-like form they pass into the equatorial plane of the spindle. Here, instead of lying in the transverse plane, their long axis lies at right angles to it, or in other words, in the same plane as the long axis of the spindle (Plate IX., Fig. 11).

This difference in the "lie" of the chromosomes is one of the most typical features of the heterotype mode of nuclear division. A second transverse division now occurs across the ring-shaped chromosomes, each half-ring being gradually drawn upwards towards its corresponding pole (Plate IX., Fig. 12). This appears to be brought about by a gradual opening out of the ring-shaped chromosomes, and in a fortunate section they may be seen straggling up along the "mantle" fibres of the spindle towards the poles of the spindle. This terminates the "heterotype metaphase."

Having arrived at the poles the chromosomes aggregate together to a certain extent, but much less so than is the case in somatic division, and almost immediately after complete division of the cytoplasm each daughter nucleus with its now permanently halved number of chromosomes begins to divide again by what is known as the "homotype" or "post-heterotype" mode of nuclear division.

This takes place as follows :—

Homotype Division.

Reference has been made to the longitudinal cleavage observable in the chromatic thread of the heterotype prophase

(Plate IX., Fig. 8). This cleavage, which represents the normal somatic cleavage, appears to be held in abeyance throughout the heterotype division, but its presence is detectable in the heterotype chromosomes more or less throughout all the various heterotype phases.

As the heterotype chromosomes pass towards the poles of the spindle it becomes much more obvious, and when anaphase is reached this longitudinal split appears to open out, producing the appearance indicated in Plate IX., Fig. 13.

When the homotype division begins it does so by the medium of this cleavage through a series of mitotic figures similar to those occurring in somatic division, but with the important difference of having only half the number of chromosomes which were contained in the somatic cell (Plate IX., Fig. 14).

Thus it would appear that the homotype division concludes a process begun very early in the heterotype prophase, but which has been, so to speak, "shelved" by the insertion of a different series of phases terminating in the reduction of the number of chromosomes to half the somatic number.

In the higher animals homotype division only occurs once, and concludes the formation of the mature ovum or spermatozoon.

But in all but the highest plants it is repeated many times, and the result of this division is the production of the "prothallus," "gametophyte," or sexual generation of the plant.

Hence, as Professor Farmer has pointed out, this single homotype division of the animal cell corresponds fundamentally to a prothallic generation, although the large and multicellular prothallus of ferns is represented in the animal kingdom by a "prothallus" consisting of a single cell.

The egg cell and the spermatozoon therefore represent cells whose "chromosome content" is reduced to half the number of that of the somatic cell.

When conjugation between the male and female elements occurs, the somatic number of chromosomes is restored to the fertilized ovum and the embryo develops therefrom by a series of somatic divisions.

Such in brief, then, are the phases through which the cells of

animals and plants pass when subject to indirect division, and a study of them will at once make apparent the extreme importance of Farmer, Moore, and Walker's discovery that heterotype and homotype division is met with in malignant growths.

These authors, it should be pointed out, have carefully abstained from drawing any definite conclusions from their discovery, but have contented themselves with merely pointing out its occurrence, and suggesting an analogy between it and the production of the prothallus of plants.

Bashford has developed some of the very obvious suggestions which arise from this discovery into a more concrete form, and has already brought forward some evidence to shew that nuclear conjugation may occur in the cells of the malignant tumours met with in some animals, but the whole matter is under consideration and investigation and at present lacks convincing proof.

The Cytology of Papilliferous Ovarian Cysts.

The number of specimens I have investigated is three. The bulk of the materials were fixed by a short exposure to the action of acetic alcohol, but part of the tumour obtained from the last case was fixed in Flemming's strong solution.

Various staining methods have been tried. The best results were obtained with iron hæmatoxylin, but Flemming's triple stain and such aniline dyes as aniline gentian violet and basic fuchsin were also tried.

Specimen 1 was obtained from a woman aged 45. Only one ovary was affected. Macroscopically it consisted of a multilocular cyst of the oöphoron (probably), the cyst spaces being filled with a soft papillomatous growth sprouting from the cyst walls and supported by a central and branching stem of connective tissue. The intracystic papillomata had burst through the wall of the cyst and had become adherent to the parts around.

Microscopically the growth shewed a single layer of columnar epithelium surrounding a core composed of connective-tissue cells.

Divisions were sparsely observed and in all instances were of the somatic type. Not a single heterotype division was found during an examination of many slides from different parts of the growth.

Judged by the ordinary standards this growth was an innocent one, and the additional aid lent by cytology confirmed the view.

Specimens 2 and 3 were removed from two patients each aged 55 years. Only a single ovary in either case was affected.

On macroscopic examination the features presented by them were very similar to those seen in Case I., except that the intracystic growths were rather softer and the tumours larger. Both growths had ruptured through the cyst walls and had become adherent to the peritoneum, but there was no general peritoneal dissemination in either case.

Microscopically they differed from No. 1 in the great number of layers of epithelial cells which clothed the connective-tissue stalk. The cells were large and spheroidal in outline.

The history in both cases was a short one, and the growths were held to be malignant at the time of removal. In these two specimens enormous numbers of mitotic figures were observable, the most striking and characteristic of which have been reproduced in the composite drawing constituting Plate X. The figures therein delineated are not diagrammatic, but were drawn by camera lucida under a magnification of 1,500 diameters.

It must be remembered in studying such drawings that each one as a rule represents several microscopical planes, since it is comparatively rare to obtain all the essential features of the nucleus in one plane, the cells being most commonly cut across with various degrees of obliquity.

An examination of the mitoses occurring in these two papilliferous cysts, which as I have already pointed out had the clinical and pathological aspects of malignancy, confirms the observations of Farmer, Moore and Walker, for the feature of the sections was the presence of heterotype and homotype mitoses in abundance, together with certain large multipolar forms of division.

A detailed description of the karyokinetic figures is not called for, but a reference to Plate X. will illustrate the important features.

The two most conspicuous objects are drawn in Figs. 1 and 2 (Plate X.). They are nuclei in the metaphase of the heterotype and homotype division respectively.

The distinction between these two when viewed from the side is not always easy, because there is a tendency to overstain this phase, and then the equatorial plate of chromosomes appears almost as an homogeneous object. In lightly stained specimens the distinction between the short V-shaped chromosomes in the equatorial plane of the homotype, and the ovate more solid-looking masses of the heterotype chromosomes arranged at right angles to the equatorial plane, is very noticeable.

When these chromosomes were counted they were found to contain the reduced number, numbers varying between 13 and 16 being obtained.

It must be pointed out that as sections frequently cut across a cell the full number of chromosomes is often absent from one section of the cell, but the distinction between numbers approximating to 16 and 32 respectively is so gross as not to lead to confusion between the two main types of division.

If serial sections be examined, the full number of chromosomes corresponding to normal and reduced division respectively is found.

Fig. 3 represents a very fortunate half section of heterotype metaphase in the longitudinal direction, in which eight of the ovate chromosomes are well seen upon the nuclear spindle; one centrosome is clearly visible, as well as the ray fibres connected with it.

This figure should be compared with Fig. 4, which is a typical somatic metaphase viewed from the side, but somewhat obliquely. The large number of chromosomes (32) and their more delicate and rod-like shape is indicated, and it will be seen that in it the chromosomes lie in the equatorial plane of the spindle, whilst in Figs. 1 and 3 they lie at right angles to that plane.

Figs. 5 and 6 are drawn from polar views of somatic and heterotype metaphases respectively. In Fig. 5 the numerous and delicate V-shaped chromosomes present a great contrast to the less numerous and coarser half loops of the heterotype division shewn in Fig. 6.

Fig. 6 also shews the beginning of that longitudinal split in the heterotype half loop chromosomes which is so very characteristic of the later heterotype mitoses, and which, as I have already pointed out, is the beginning of the homotype division.

Figs. 7 and 8 are somatic and heterotype prophases.

In Fig. 7 the somatic prophase is seen ; in Fig. 8 the massive ring-shaped chromosomes form conspicuous objects, which when seen are typical of heterotype division.

Fig. 8 is a late stage of heterotype prophase, but Figs. 9, 10, 11, and 12 are drawn from the earlier conditions of the same phase.

The complicated and sharply-angled chromatic thread is indicated, and the tendency to polarisation of the thread work to one part of the nucleus (Synapses of Moore) is well seen.

Fig. 13 is another polar view of a late heterotype metaphase exhibiting longitudinal splitting of the half loop chromosomes, whilst Figs. 14 and 15 are fortunate sections which shew how the heterotype chromosomes pass up the "mantle fibres" after the transverse splitting and opening out of the loop chromosomes has taken place.

The longitudinal lie of the chromosomes on the spindle fibres should be noticed.

Figs. 16 and 17 are probably the very termination of somatic and homotype prophases respectively, the V-shaped chromosomes having been formed but not yet having begun to travel along the nuclear spindle. The reduced number of the homotype chromosomes is well seen.

Figs. 18, 19, 20, and 21 are multipolar mitoses in various phases, 18 being most probably an early heterotype prophase, and 20 and 21 metaphases which are most probably homotypical.

Fig. 19 is difficult to place. From its great size and the extreme coarseness of its chromatin thread, it is probably some abnormal condition of heterotype prophase. The chromatic threadwork appears to exhibit the longitudinal split.

Fig. 22 is an homotype anaphase, whilst Fig. 23 is a good example of telophase, in this case also probably homotypical.

Fig. 24 is another heterotype amphiaster in which two loop chromosomes appear to be beginning to divide. The centrosome and polar rays are well seen in this cell.

Between the cells undergoing mitotic division are seen many resting nuclei.

From the very large number of homotype divisions seen in these sections it would appear probable that this form of division occurs through many generations of cells (thus conforming to the vegetable type), and not on one occasion only, as is the rule in the normal generative cell formation of animals.

As regards the occurrence of heterotype and homotype mitoses in the new growths under consideration, it is a noticeable fact that the divisions appear to take place in groups, but without any definite order in the cell masses, and without reference to the position of the cells in the growth or to the age of the different parts of the tumour.

Thus the malignancy of the new growth cannot be said to depend upon the occurrence of the generative type of mitosis, since all its cells would appear to be equally malignant and infiltrative, whether they exhibit the somatic, heterotypical, or homotypical methods of division; indeed in transplantation experiments with mouse carcinoma the earliest divisions observed in the graft are somatic in character.

Rather would it appear that the occurrence of the generative type of mitosis indicates an assumption of more or less independent growth by the cell, in virtue of which it can assume a method of reproduction not possessed by it whilst it formed merely a part of a specialized cell group in the complex of the living body.

Thus these phenomena appear to support the theory that the "organism" of carcinoma is the epithelial cell itself, which has through some abnormal stimulus or nutritive change attained a more or less independent existence.

Bashford has described appearances of nuclear conjugation in the cells of epitheliomata occurring in mice. I have been unable to find any such appearances in any of the neoplasms I have hitherto examined.

Thus far, then, the cytological characteristics of the cells of the apparently malignant papilliferous cysts of the ovary are consonant with those proved to obtain in carcinomata and sarcomata elsewhere.

The difficulty of making a satisfactory diagnosis even by ordinary microscopical examination in these cases is well known.

I believe that cytology will give valuable aid in the direction of making a certain distinction between the malignant and innocent papilliferous cysts of the ovary.

My cases have occurred too recently to ascertain whether the operation is to be followed by recurrence. I trust to be able to detail the ultimate fate of these cases at some later date.

PLATE IX.

SOMATIC AND HETEROTYPE MITOSES (DIAGRAMMATIC).

FIG. 1.—Resting cell.
FIG. 2.—Somatic prophase.
FIG. 3.—Somatic metaphase—early. Eight longitudinally split chromosomes.
FIG. 4.—Somatic metaphase—late.
FIG. 5.—Somatic anaphase.
FIG. 6.—Somatic telophase.
FIG. 7.—Heterotype prophase—early.
FIG. 8.—Heterotype prophase illustrating the longitudinal cleavage of the chromatic thread.
FIG. 9.—Heterotype prophase—synaptic (contraction) figure.
FIG. 10.—Heterotype prophase—loop and ring chromosomes.
FIG. 11.—Heterotype metaphase, ring-shaped chromosomes lying longitudinally on the spindle.
FIG. 12.—Heterotype metaphase. Transverse splitting of ring chromosomes and passage up the spindle fibres.
FIG. 13.—Heterotype anaphase shewing opening out of longitudinal split in chromosomes.
FIG. 14.—Homotype metaphase. Note halved number of chromosomes.

PLATE X.

COMPOSITE DRAWING OBTAINED BY CAMERA LUCIDA UNDER MAGNIFICATION OF 1500 DIAMETERS.

FIG. 1.—Heterotype metaphase.
FIG. 2.—Homotype metaphase.
FIG. 3.—Heterotype metaphase. Half the figure appears in the drawing containing eight chromosomes.
FIG. 4.—Somatic metaphase—viewed from the side.
FIG. 5.—Somatic metaphase—polar view.

PLATE IX.

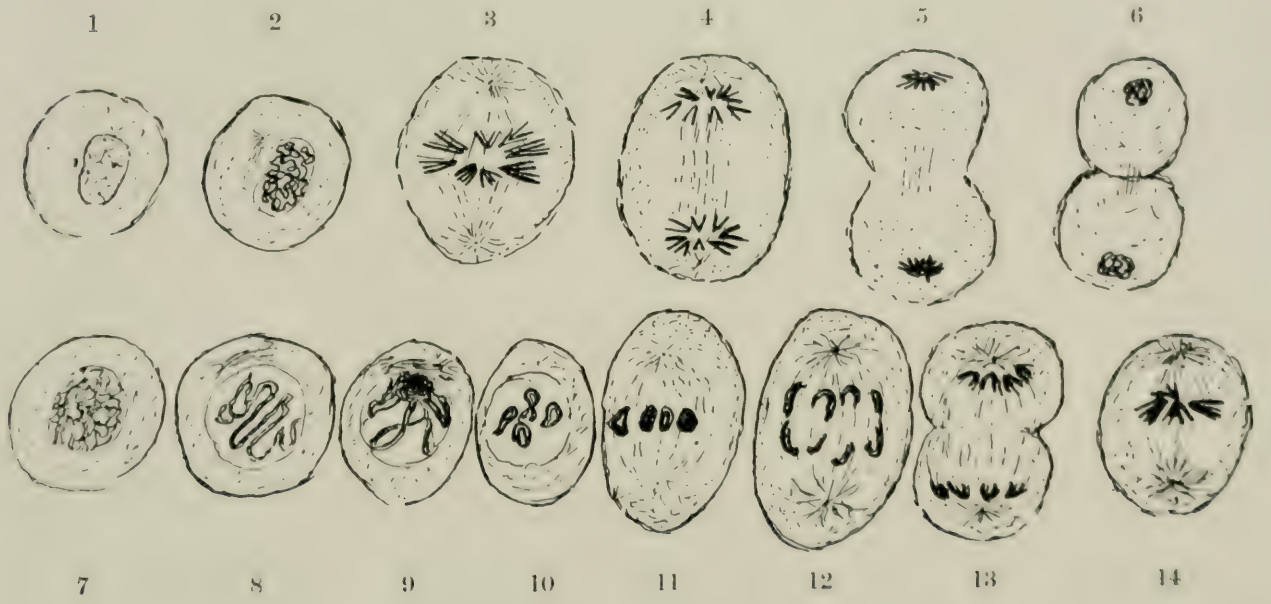

PLATE X.

FIG. 6.—Heterotype metaphase. Late stage, shewing longitudinal cleavage in the chromosomes in polar view.

FIG. 7.—Somatic prophase.

FIG. 8.—Heterotype prophase—late stage.

FIG. 9.—Heterotype prophase—early stage.

FIG. 10. } Heterotype prophases, shewing the contraction figures.
FIG. 11. }
FIG. 12. }

FIG. 13.—Heterotype metaphase—late stage, polar view.

FIG. 14. } Heterotype metaphases, shewing the loop chromosomes passing up the
FIG. 15. } spindle fibres.

FIG. 16.—Somatic prophase—late stage.

FIG. 17.—Homotype prophase—late stage, reduced number of chromosomes.

FIG. 18.—Prophase, probably early multipolar heterotype.

FIG. 19.—Prophase, probably late multipolar heterotype.

FIG. 20. } Multipolar metaphases, probably homotype.
FIG. 21. }

FIG. 22.—Homotype anaphase—side view.

FIG. 23.—Homotype telophase—side view.

FIG. 24.—Heterotype metaphase—oblique view.

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